

Fig. 1

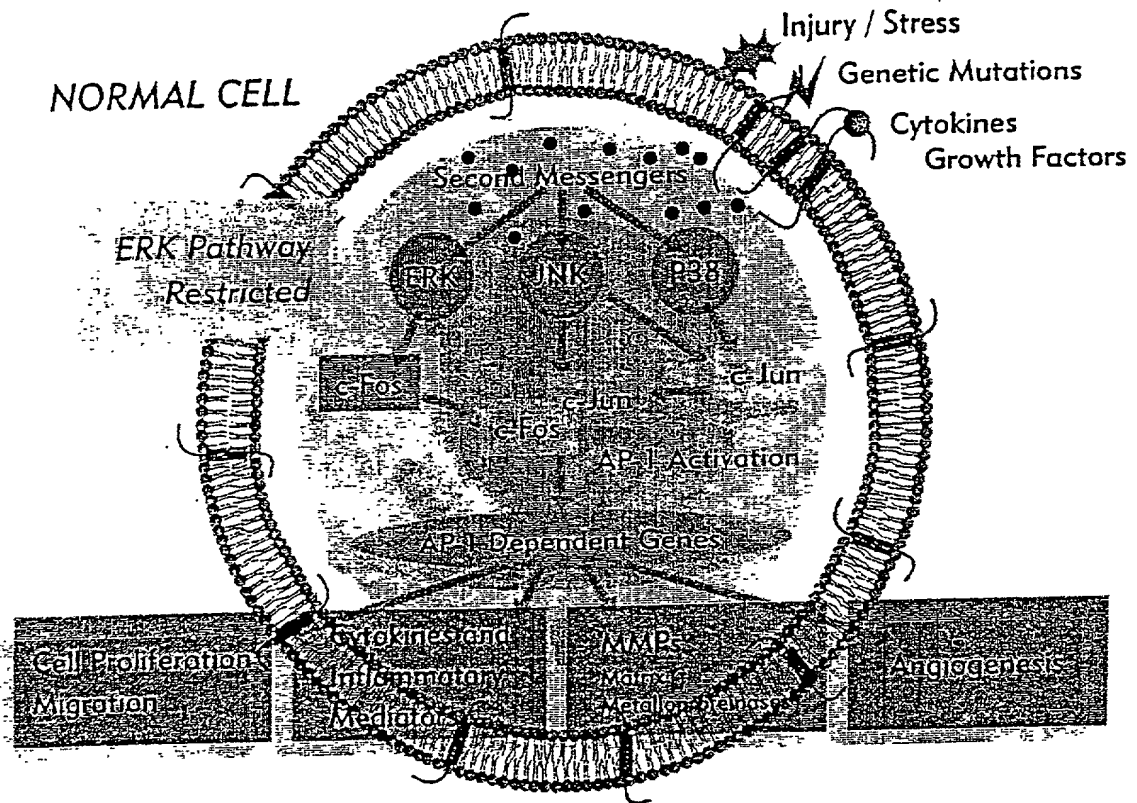


Fig. 2

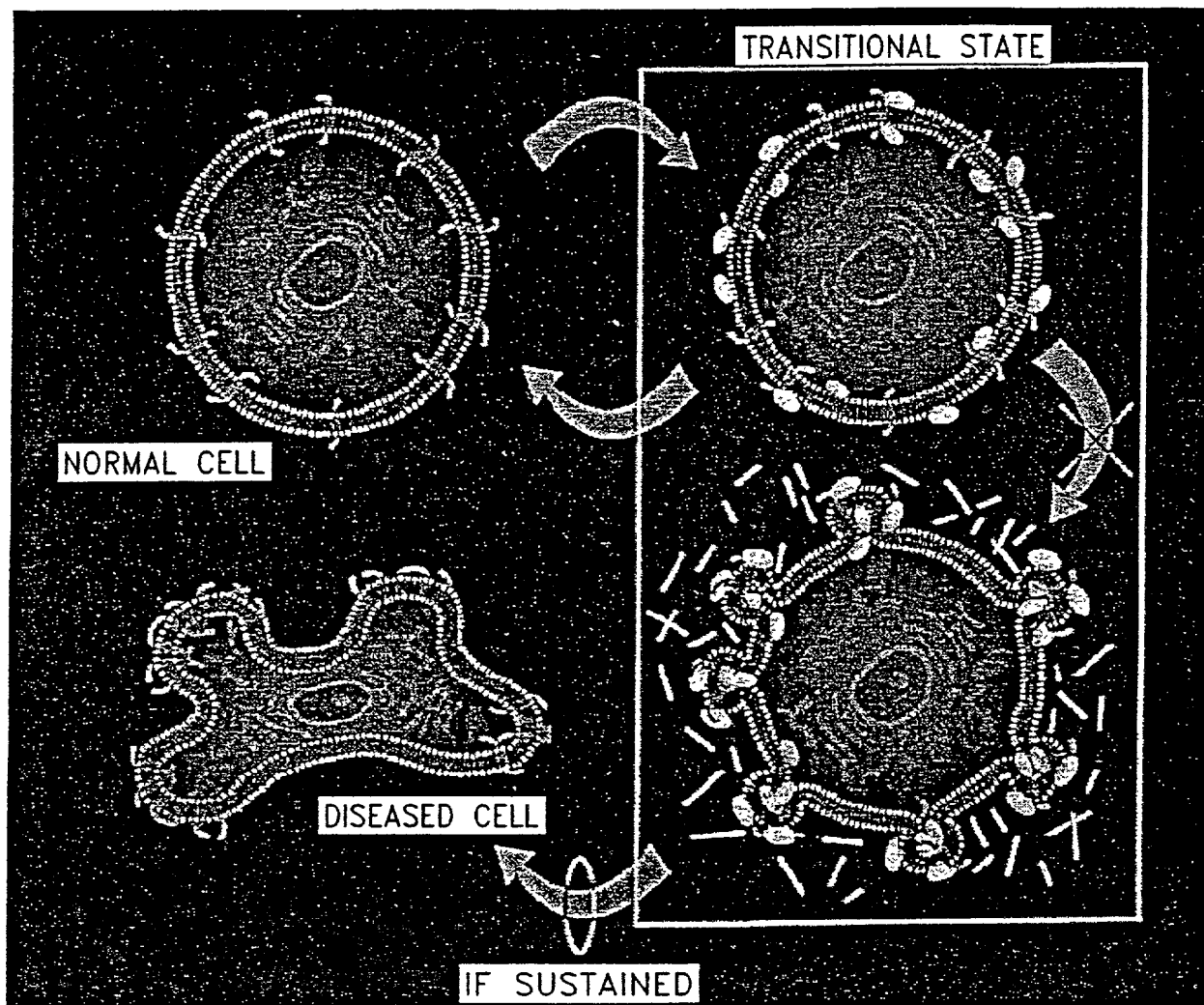
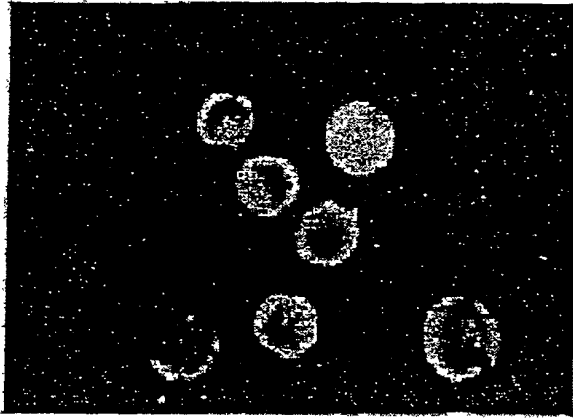
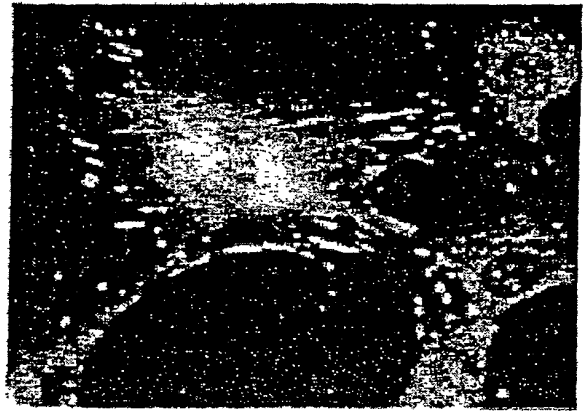


Fig. 3

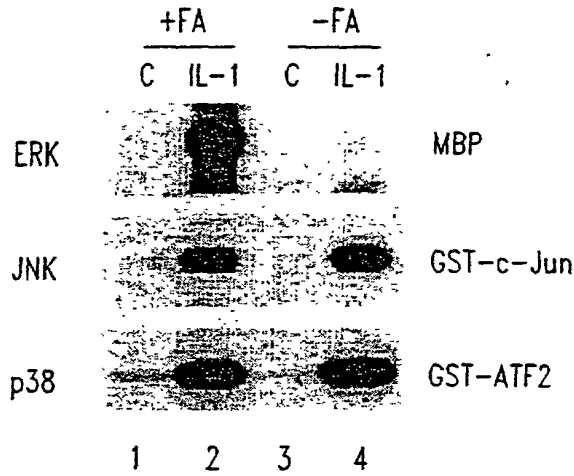
-Focal Adhesions (-FA)



+Focal Adhesions (+FA)

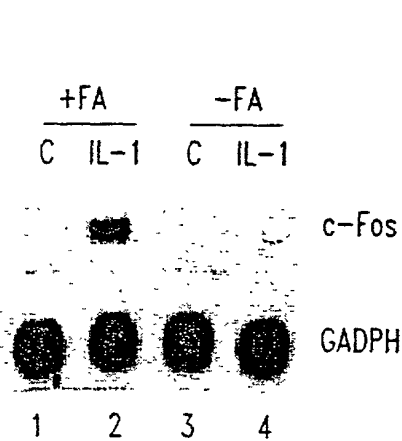


*Fig. 4A*

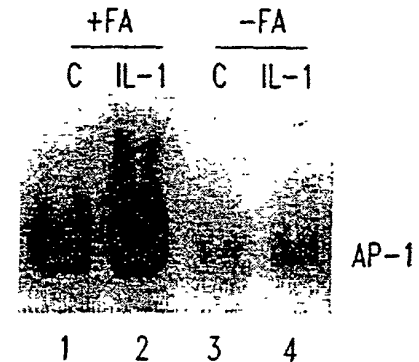


*Fig. 4B*

*Fig. 4C*

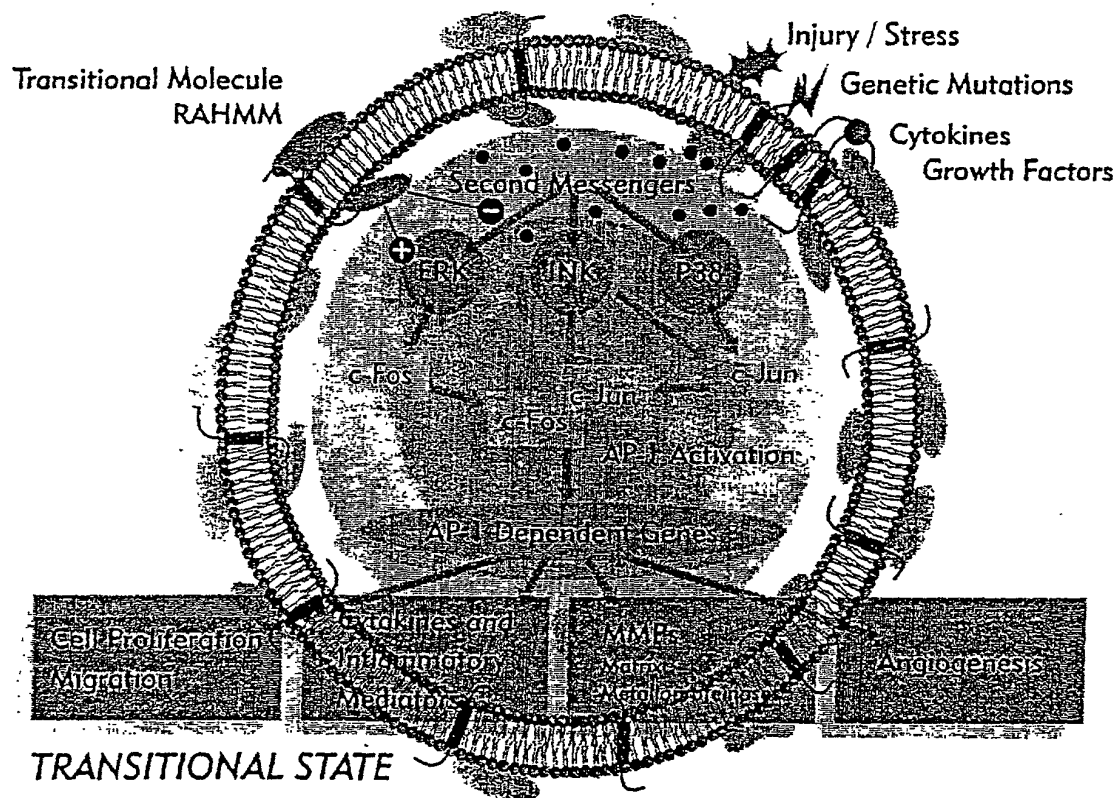


*Fig. 4D*

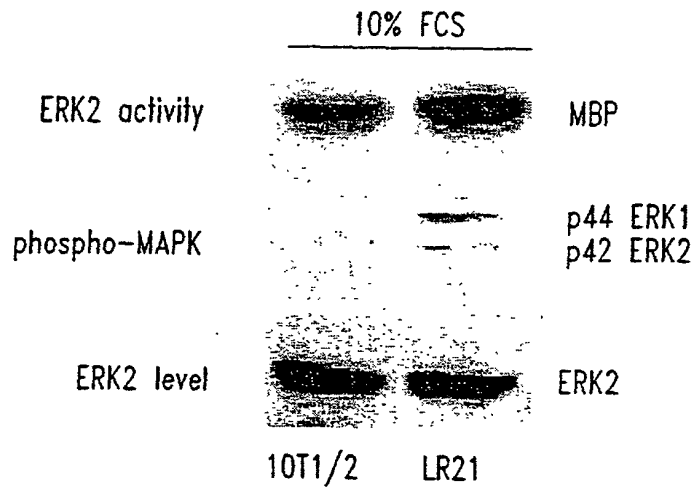


*Fig. 4E*

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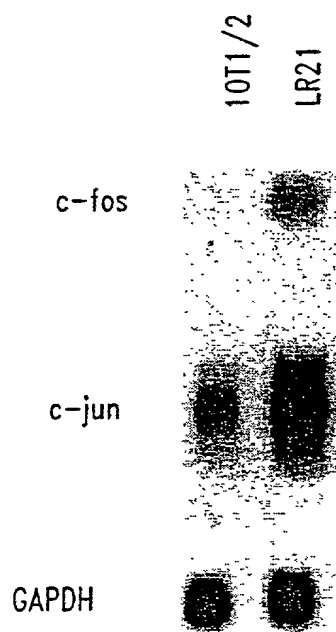
*Fig. 5*



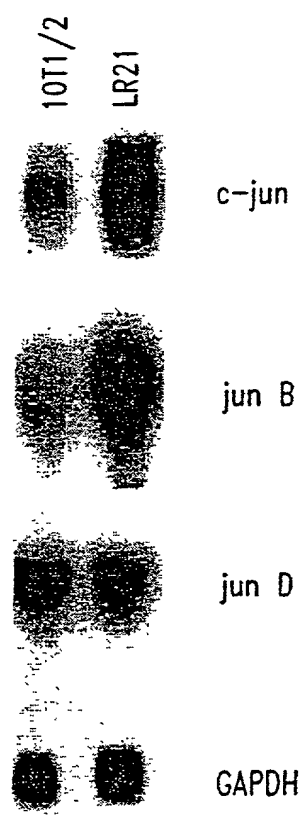
*Fig. 6A*



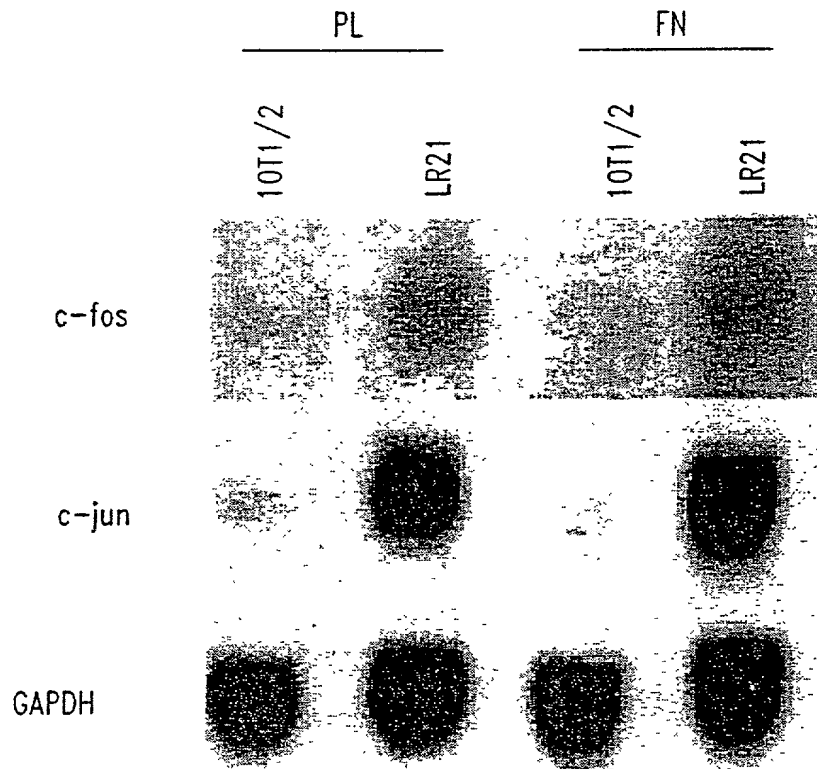
*Fig. 6B*



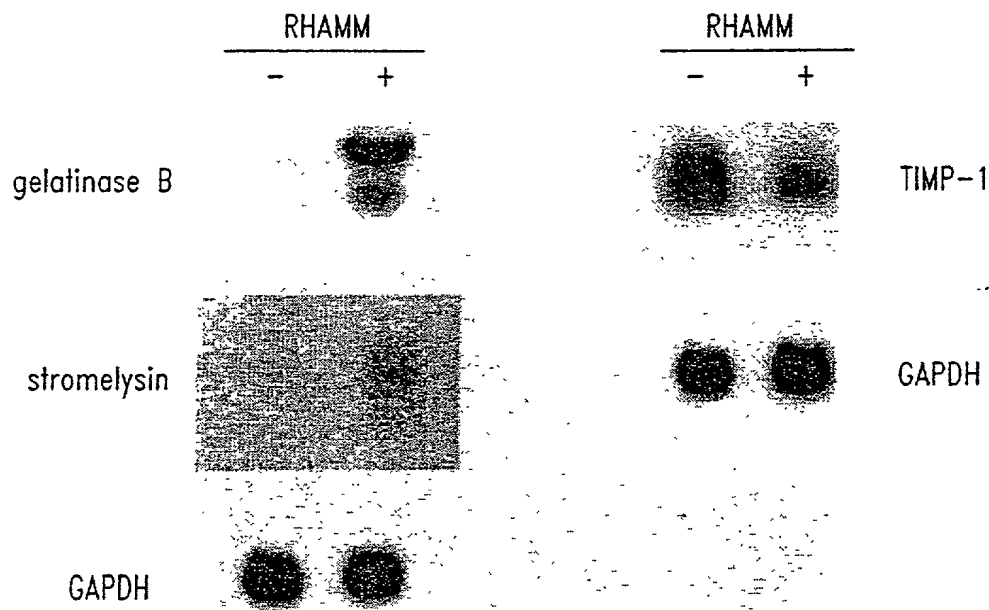
*Fig. 7A*



*Fig. 7B*

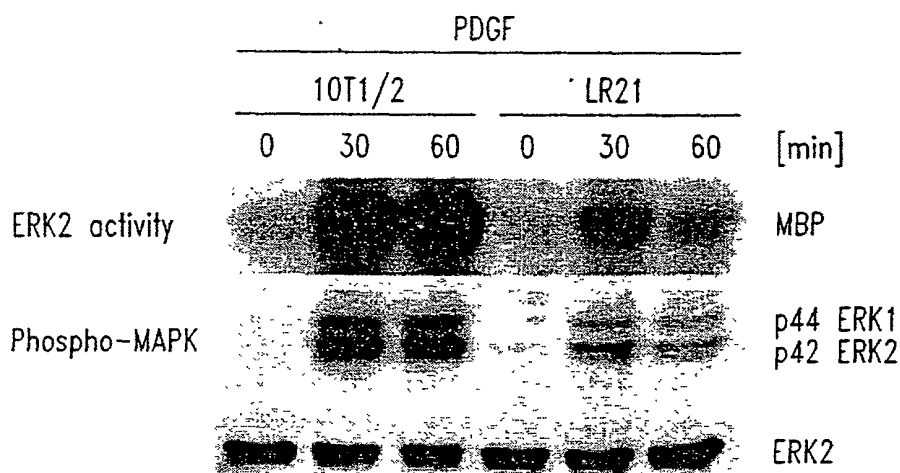


*Fig. 8*

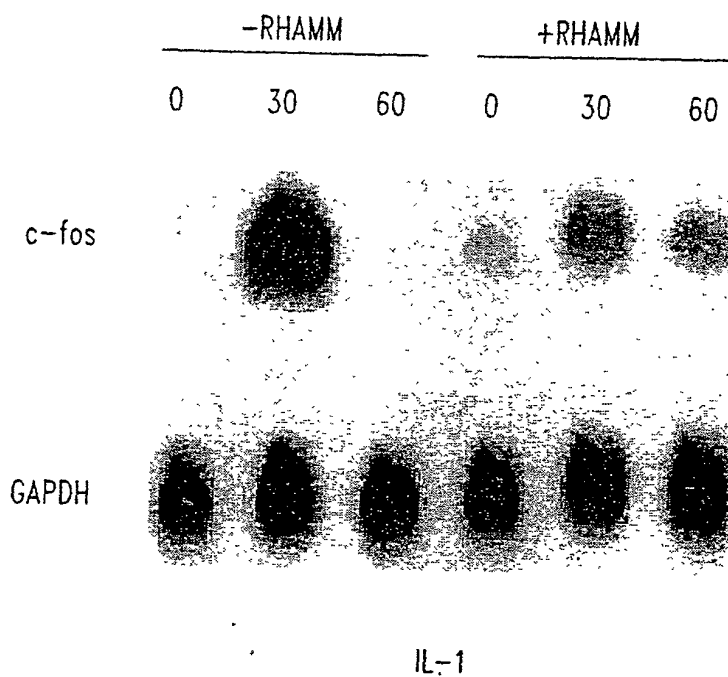


*Fig. 9*

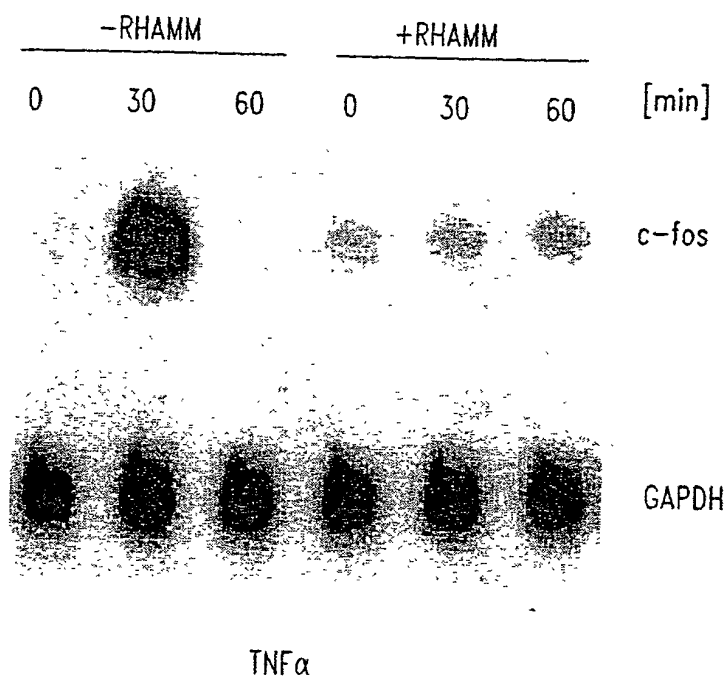




*Fig. 10*

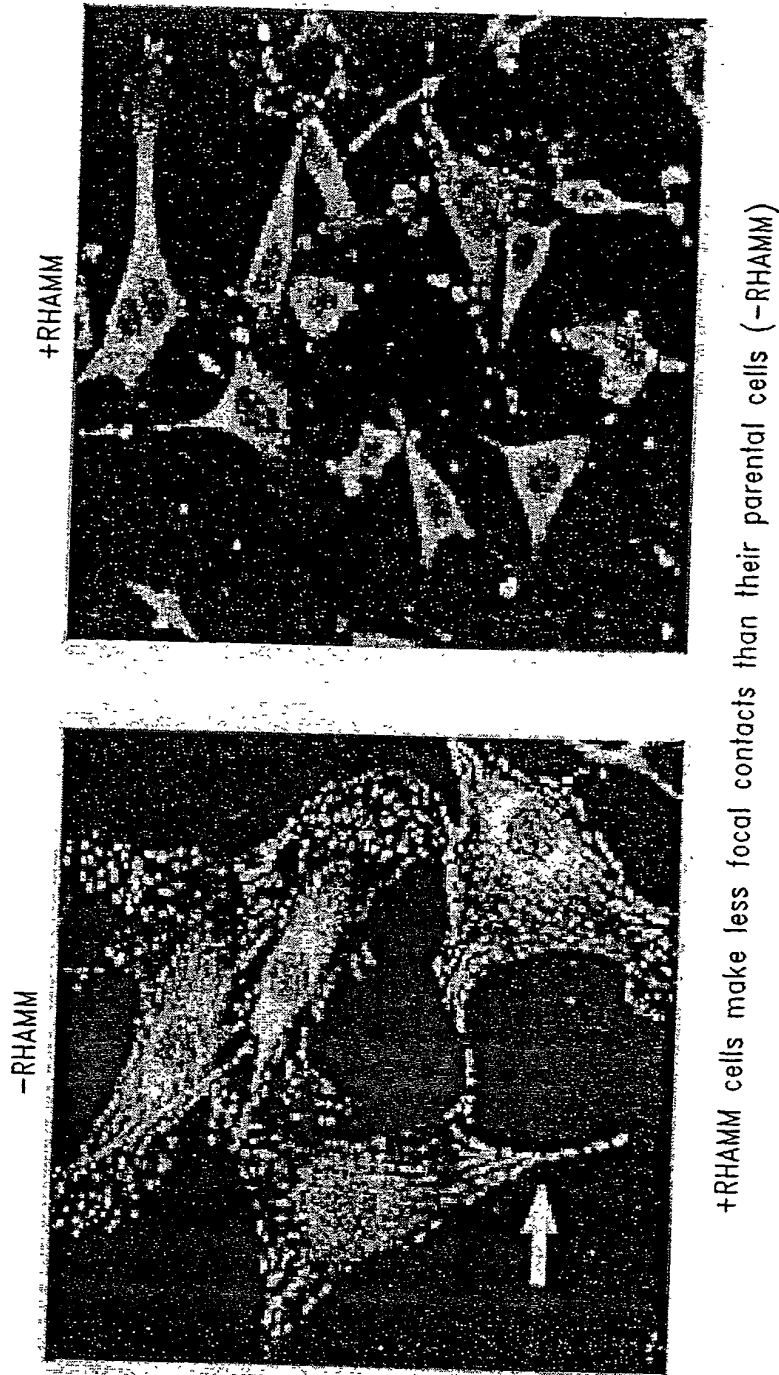


*Fig. 11A*



*Fig. 11B*

FOOTNOTES: 6022669

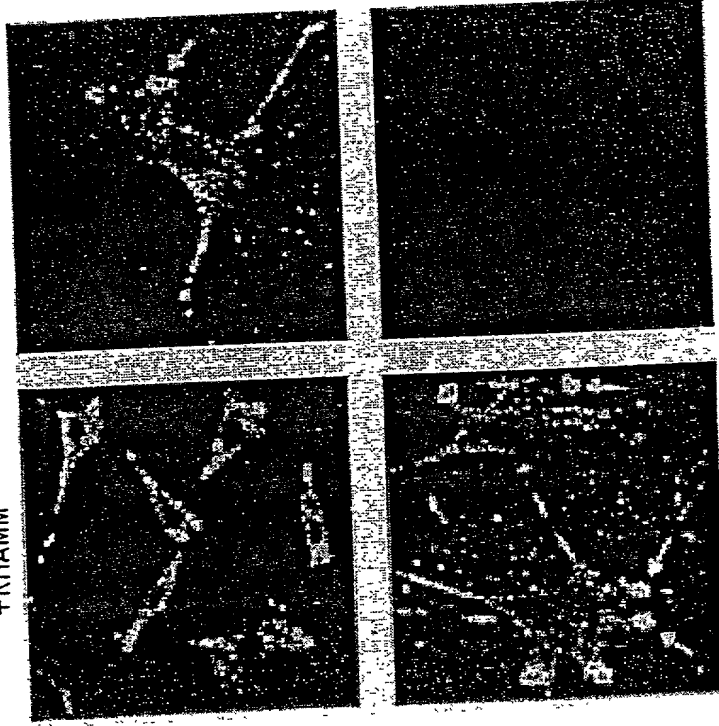


*Fig. 12A*

*Fig. 12B*

-RHAMM

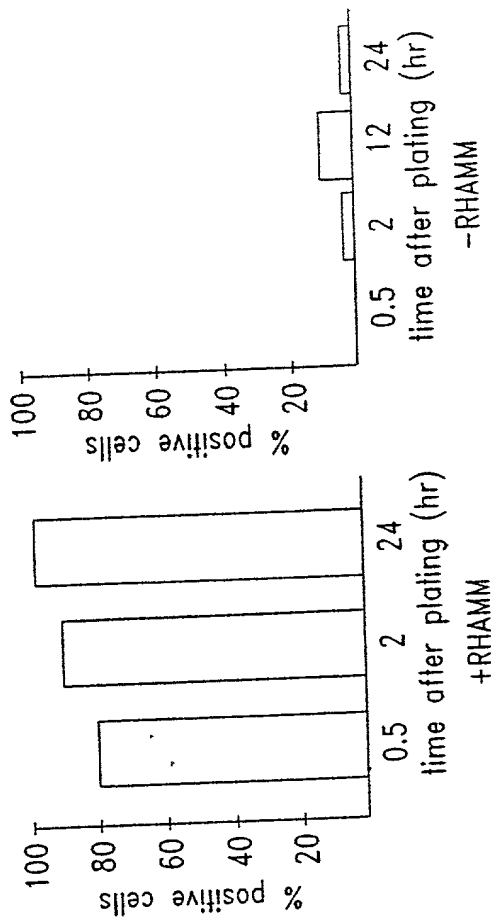
+RHAMM



6 hrs

24 hrs

- Overexpression of RHAMM results in increased and sustained production of podosomes



- In most cells responding to injury, podosomes are formed and disassembled rapidly (-RHAMM, 6 vs. 24 hrs)

Fig. 13

APPLN. FILING DATE: FILED HEREWITH

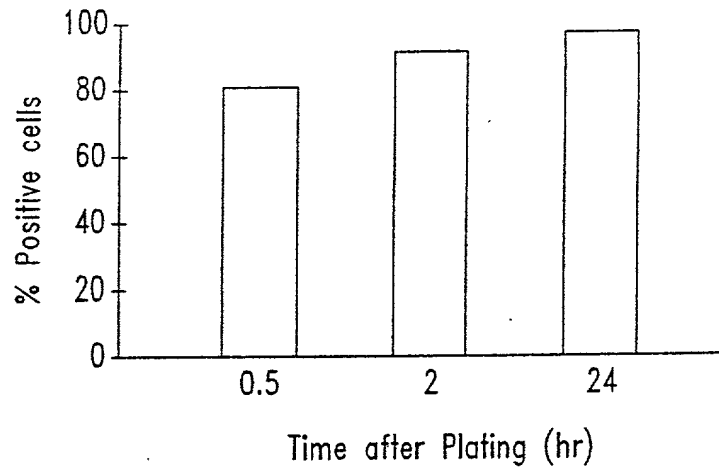
TITLE: COMPOSITIONS AND METHODS FOR

TREATING CELLULAR RESPONSE TO INJURY AND ...

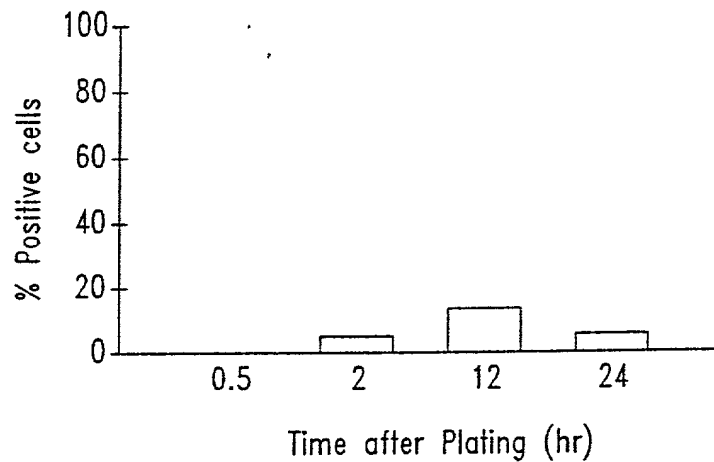
INVENTOR(S): TONY CRUZ, ET AL.

ATTORNEY DOCKET No.: 033352-010

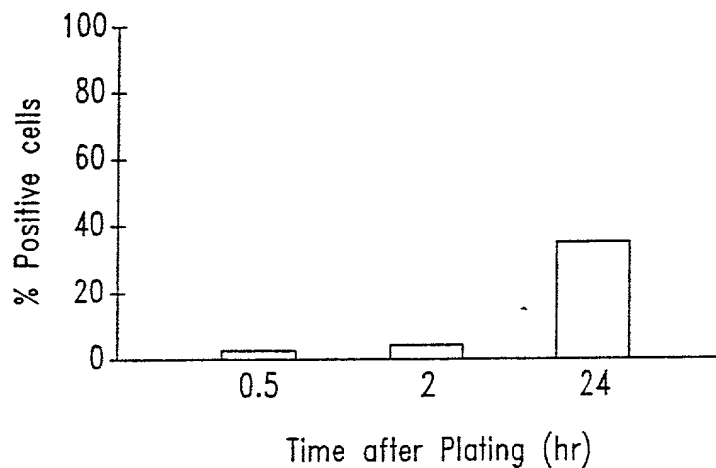
SHEET 12 of 63



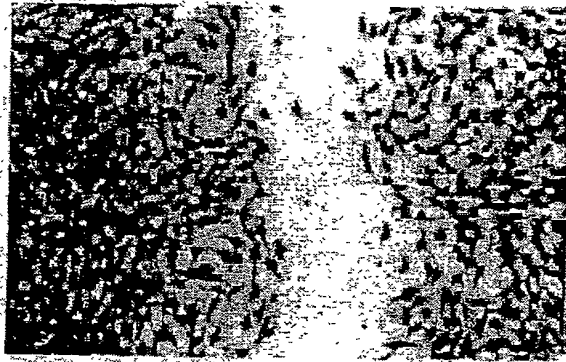
*Fig. 14A*



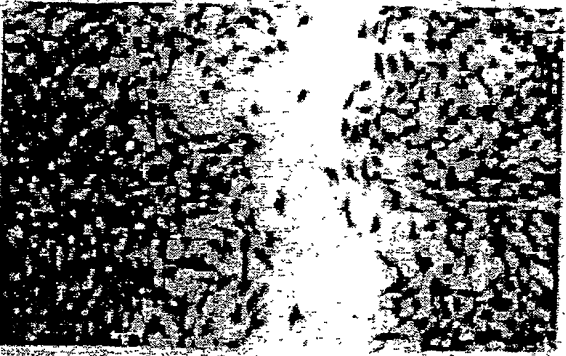
*Fig. 14B*



*Fig. 14C*



*Fig. 14F*

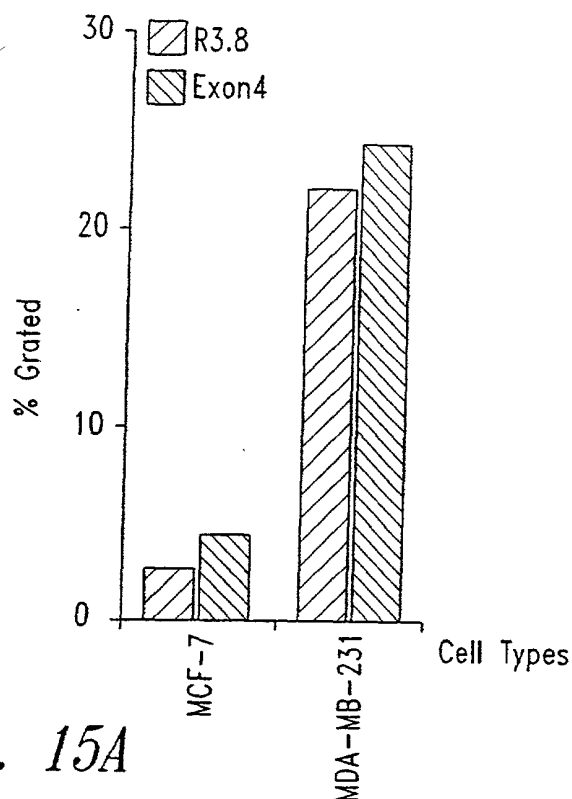


*Fig. 14E*



*Fig. 14D*

FOOT-60E92650



*Fig. 15A*

RHAMM Peptides

Murine Exon3 sequence:

N-terminal ---KLQATQKDLTESKGKIVQLEGKL--- 23aa

SEQ ID. NO. 14

For Exon3 antibody, used the peptide sequence:

(C) KLQATQKDLTESKG

SEQ ID. NO. 15

Murine Exon4 sequence:

N-terminal ---VSIEKEKIDEKCETEKLLEYIQEIS--- 25aa

SEQ ID. NO. 16

For Exon4 antibody, used the peptide sequence:

(C) VSIEKEKIDEKC/S

SEQ ID. NO. 17

For antibody to Human RHAMM v5, used the peptide sequence:

(C) LKSKFSENGNQKNL

SEQ ID. NO. 18

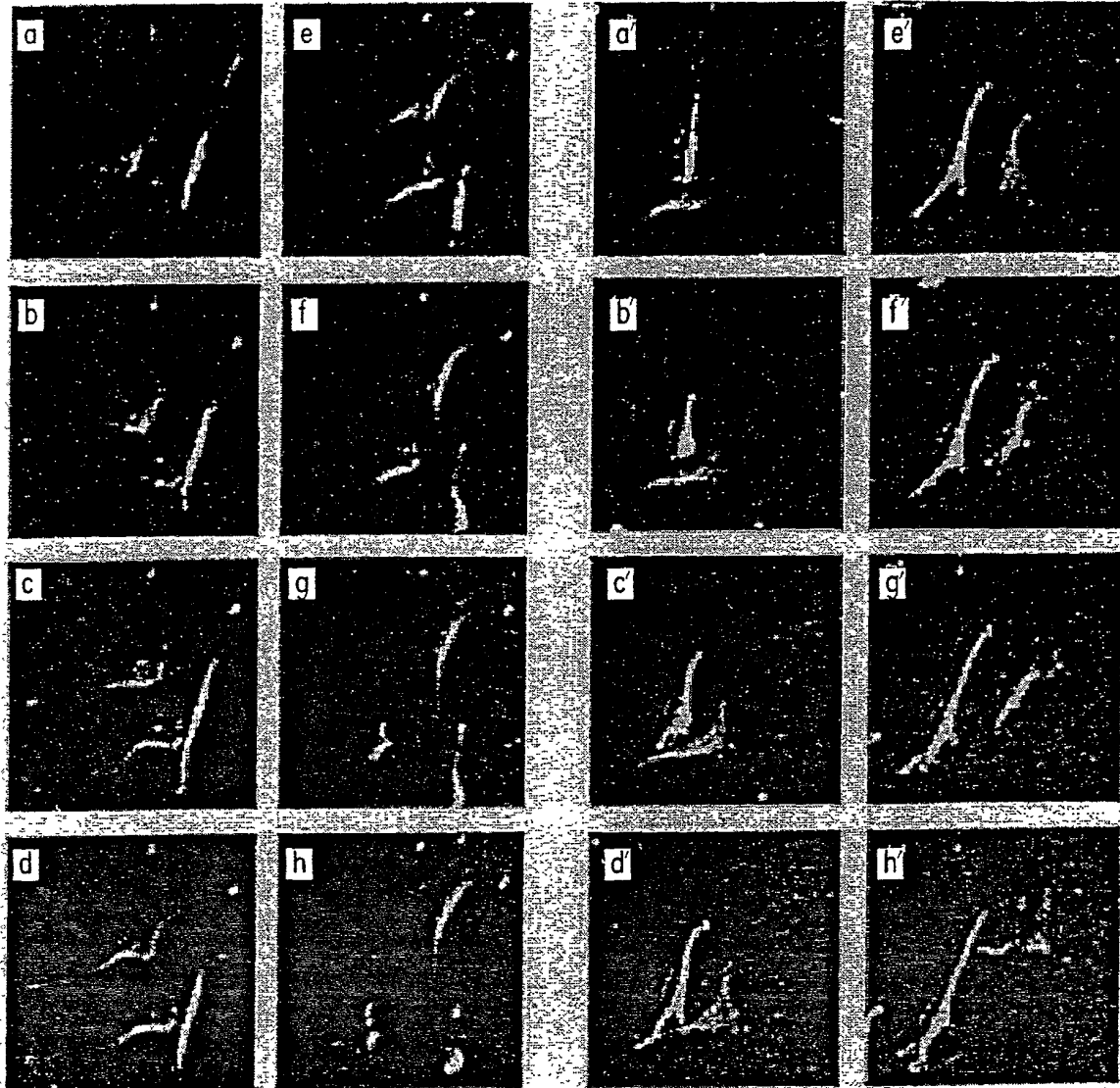
Homology between three peptides from murine (M) and human (H) RHAMM (as used to raise antibody)

1) Exon3	M:	KLQATQKDLTESKG	as in	SEQ ID. NO. 15
	H:	---V--RS-E-Q--		SEQ ID. NO. 19
2) Exon4	M:	VSIEKEKIDEKC	as in	SEQ ID. NO. 17
	H:	-----S	as in	SEQ ID. NO. 17
3) v5	M:	--A----D-H---M		SEQ ID. NO. 20
	H:	LKSKFSENGNQKNL	as in	SEQ ID. NO. 18

*Fig. 15B*

peptide 1

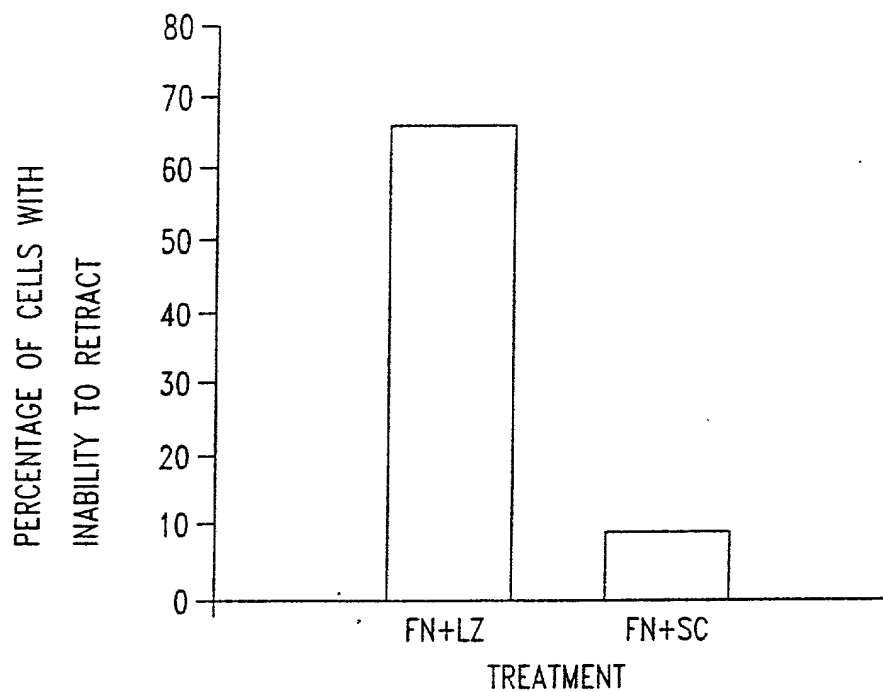
peptide 2



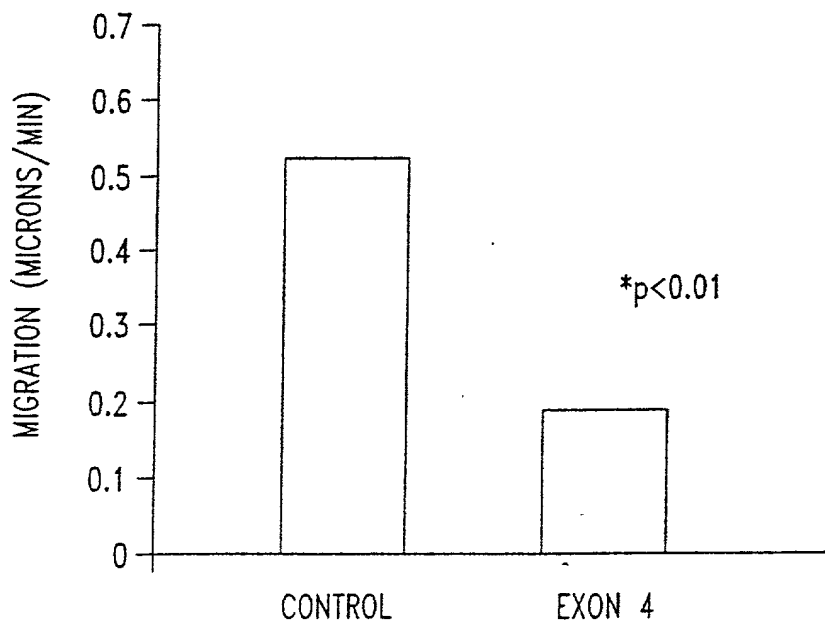
*Fig. 16A*

*Fig. 16B*

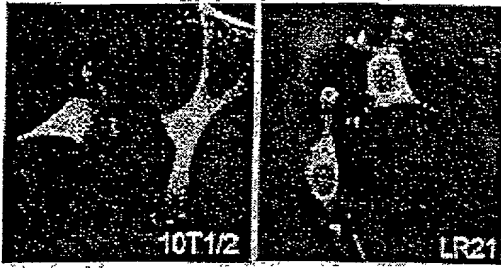




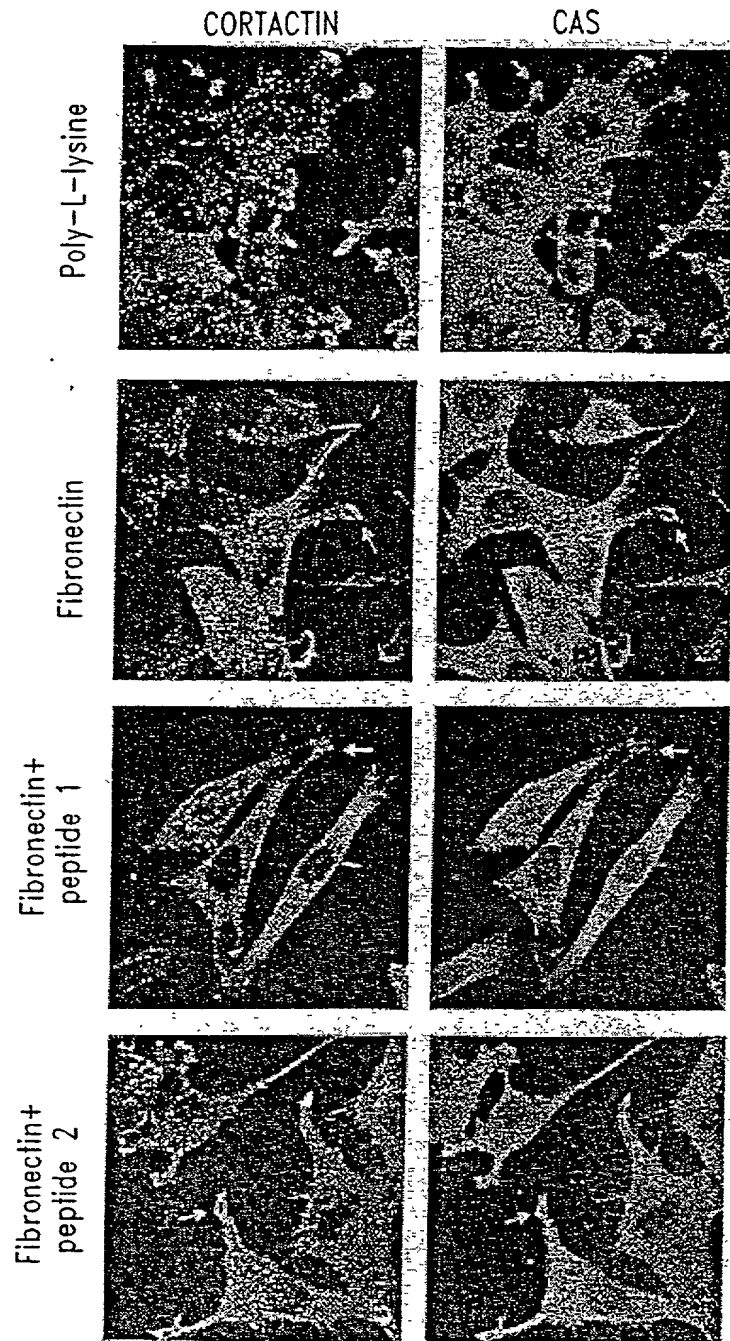
*Fig. 16C*



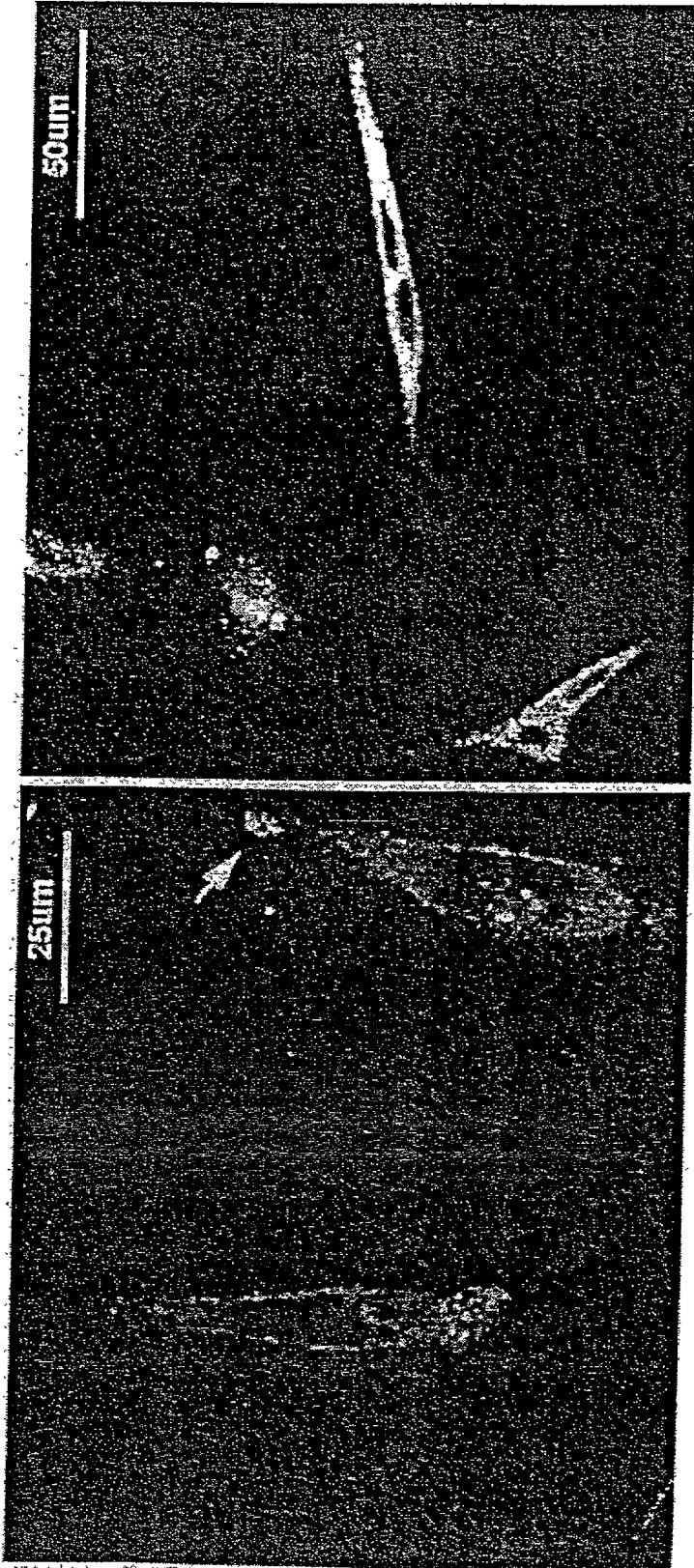
*Fig. 16D*



*Fig. 17A*



*Fig. 17B*



*Fig. 18*

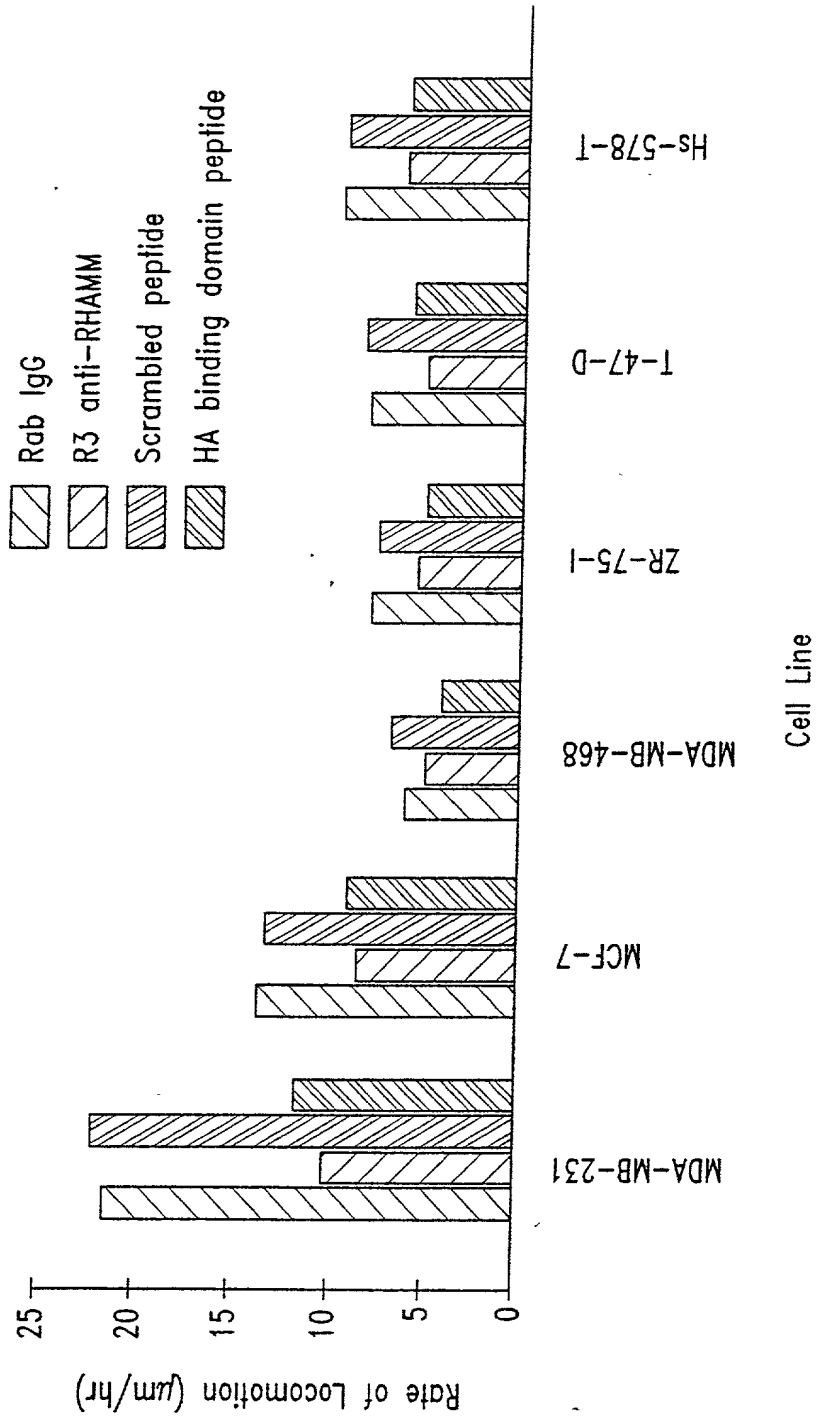
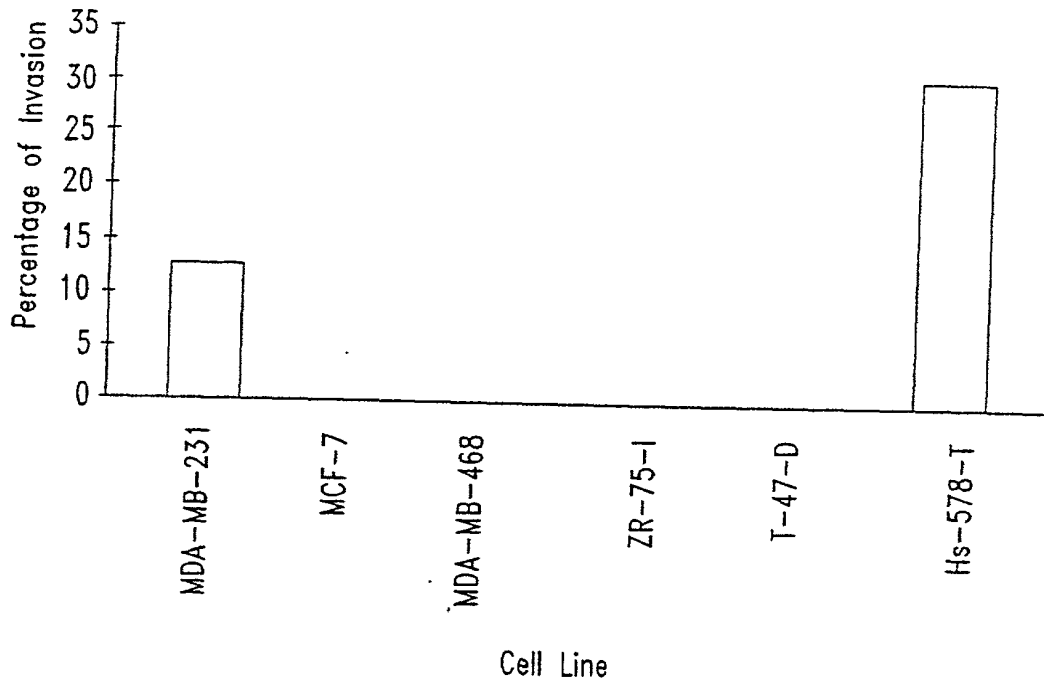
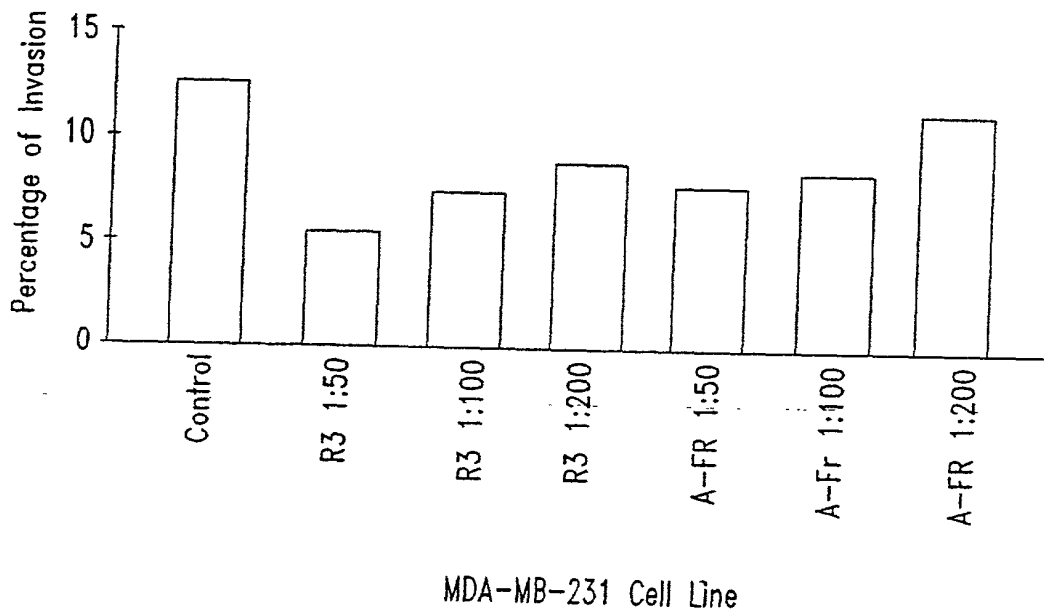


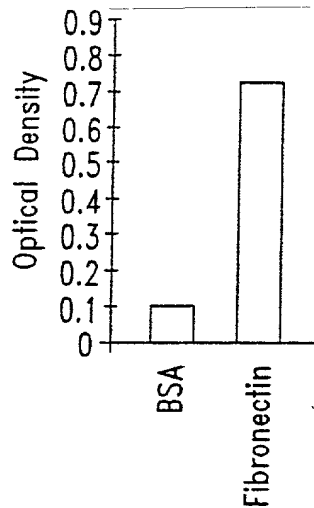
Fig. 19



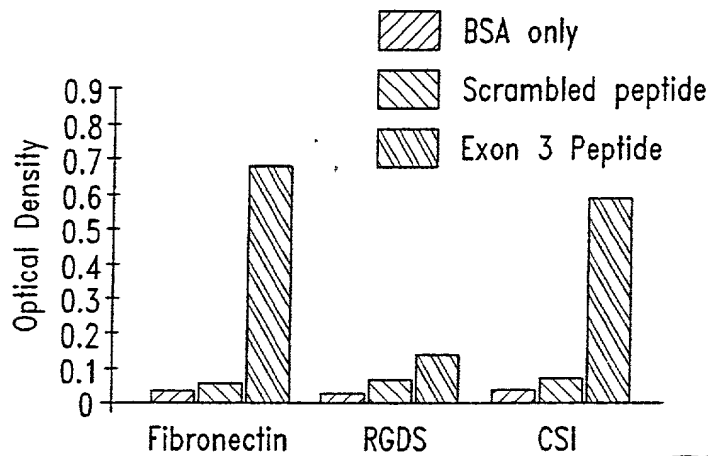
*Fig. 20A*



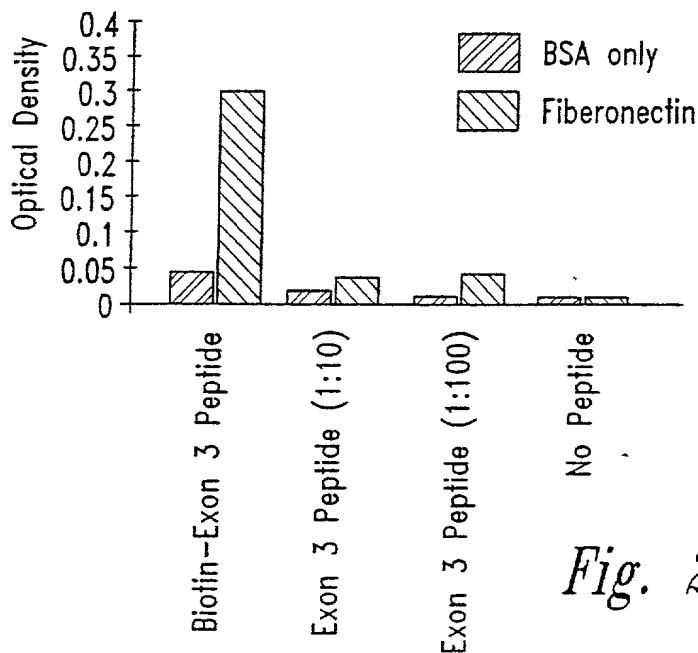
*Fig. 20B*



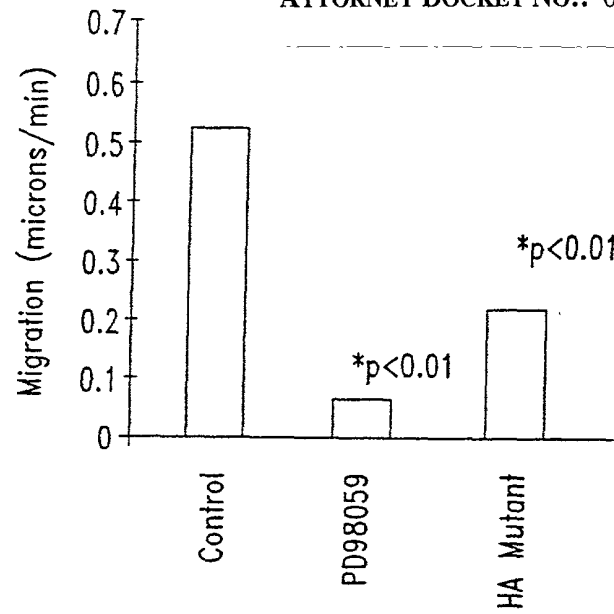
*Fig. 21A*



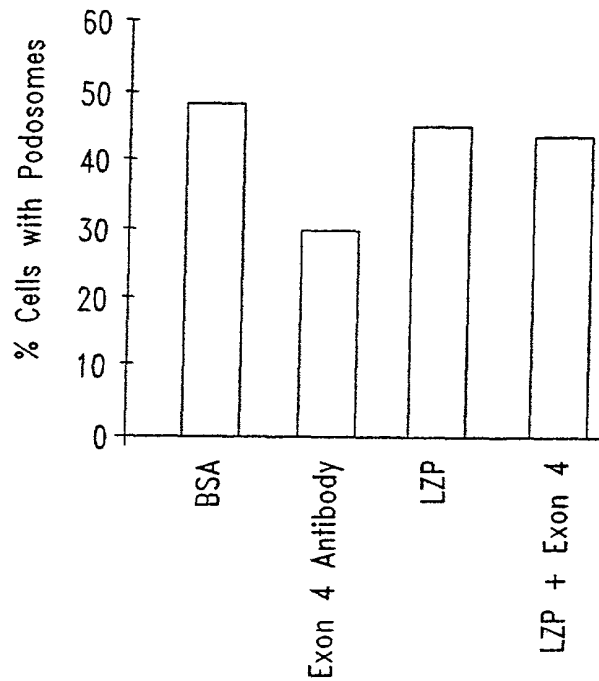
*Fig. 21B*



*Fig. 21C*

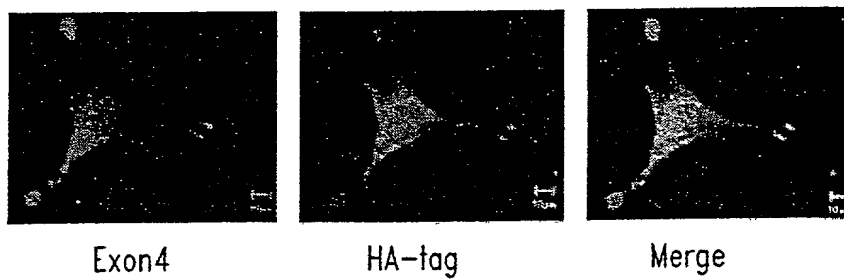


*Fig. 22*

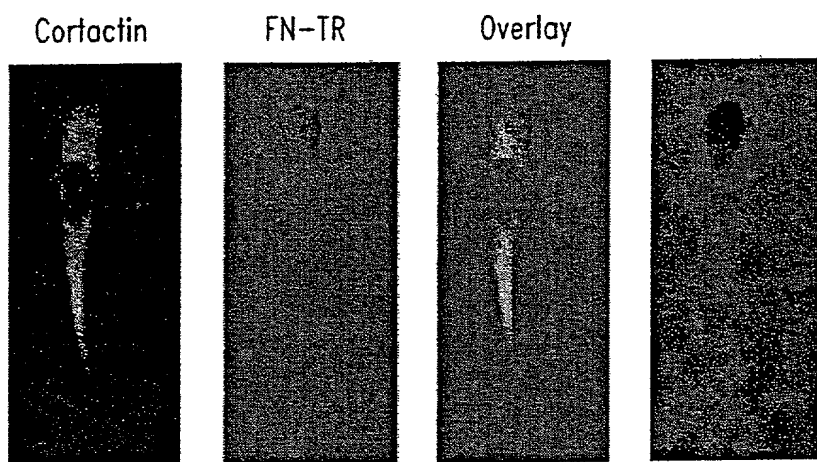


Effects of Exon4 Antibody and LYP  
 on the Podosome Formation of LR21

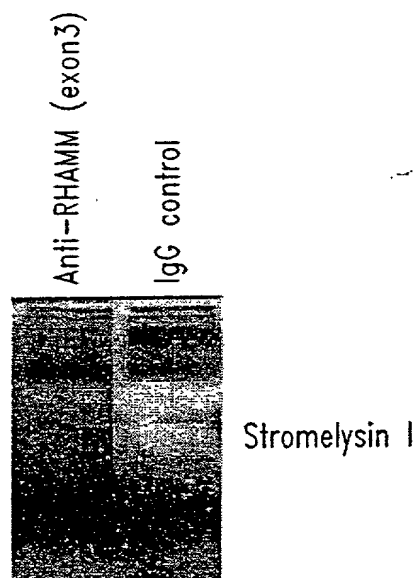
*Fig. 24A*



*Fig. 23A*



*Fig. 23B*



*Fig. 24B*

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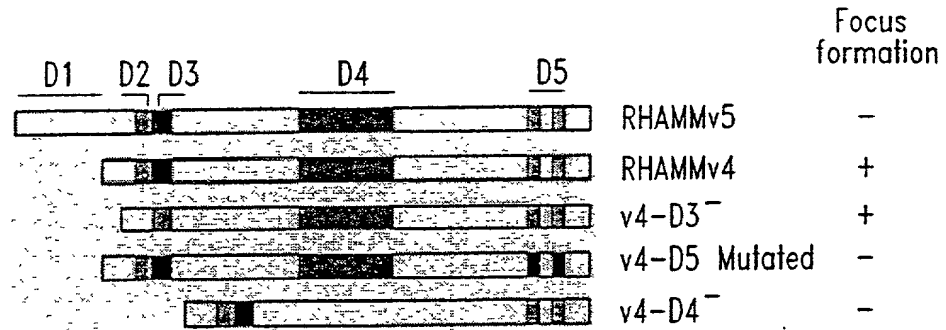


Fig. 25A

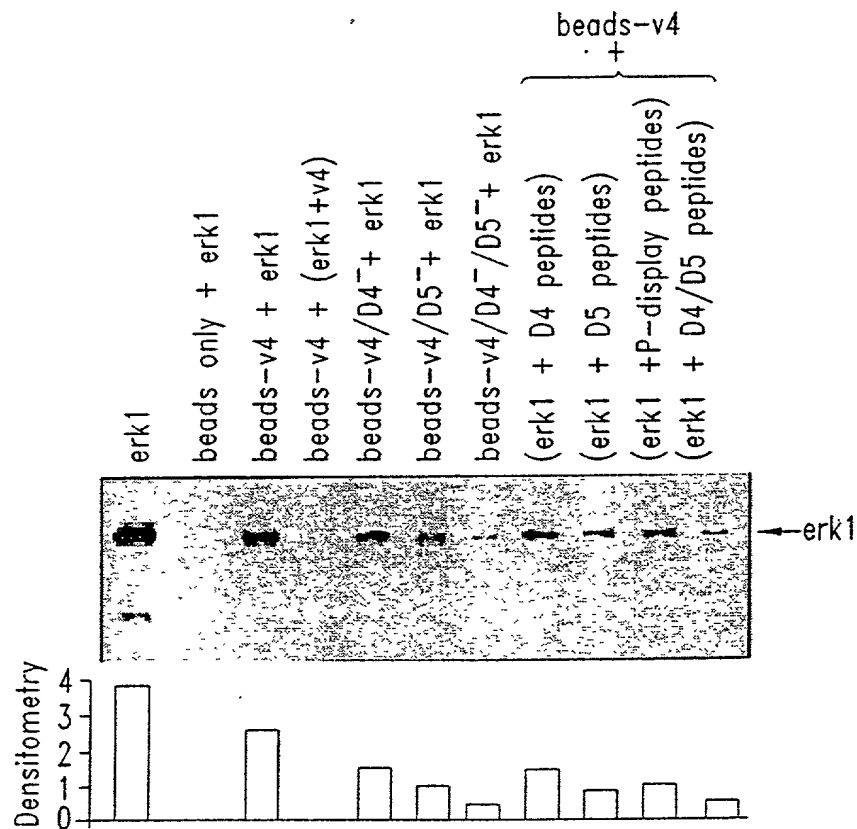


Fig. 25B

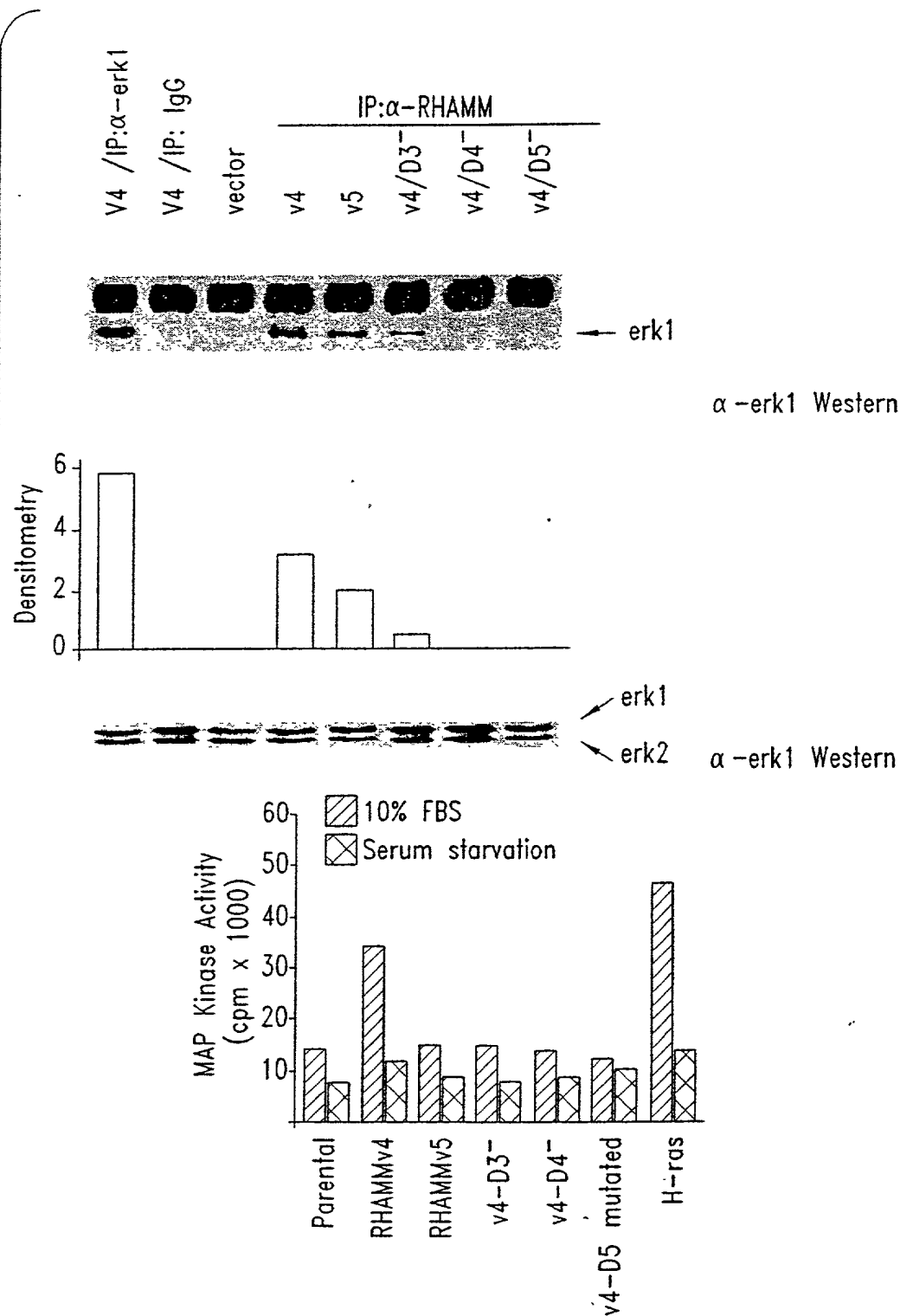
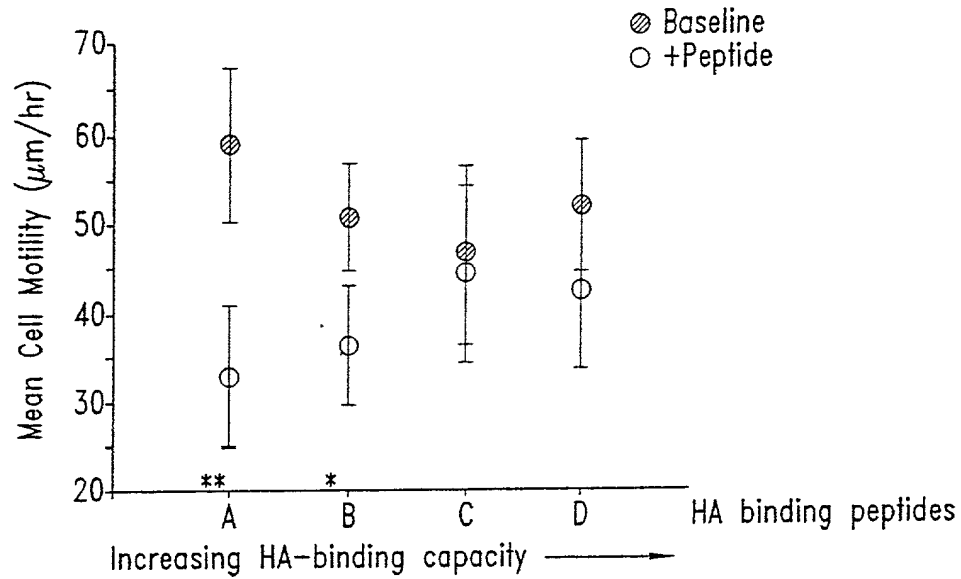


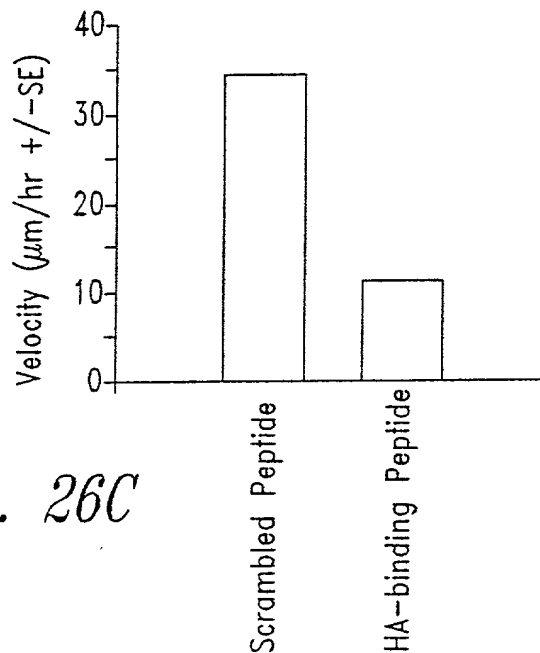
Fig. 25C

A: RGGGRGRRR  
 B: RGGGRGGRR  
 C: RGGGRGGGR  
 D: RGGGGGGGR

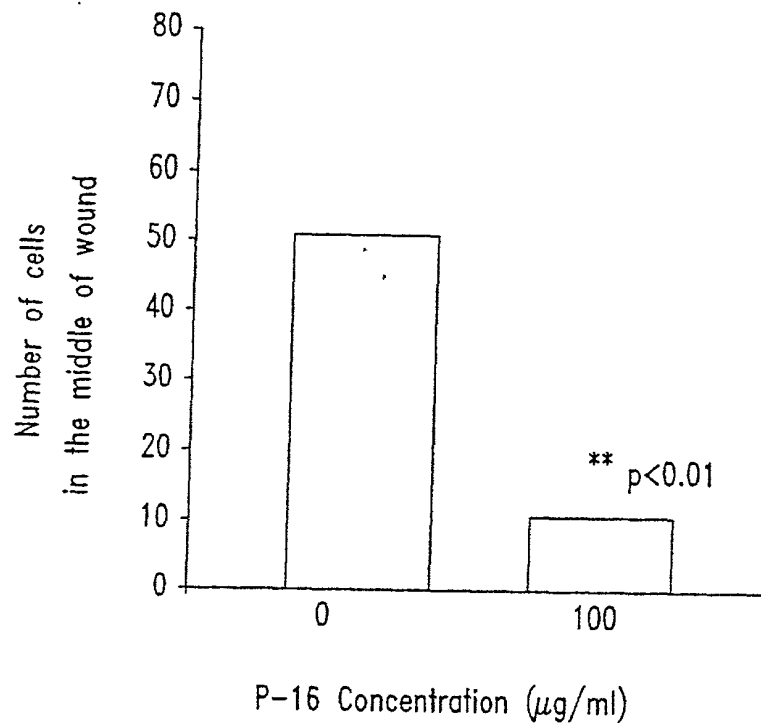
*Fig. 26A*



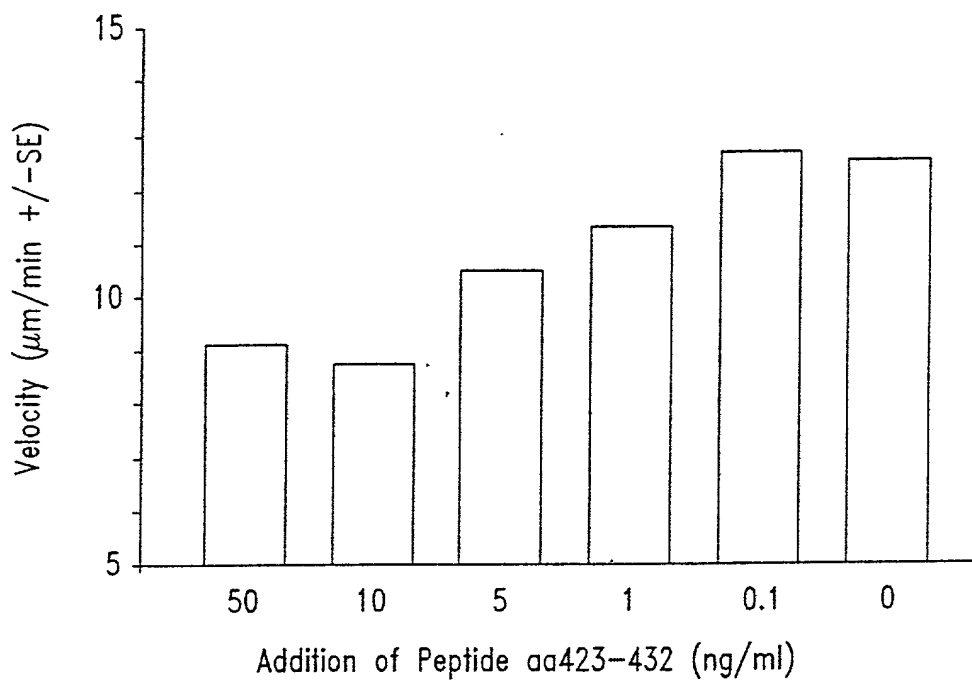
*Fig. 26B*



*Fig. 26C*



*Fig. 27*



*Fig. 28*

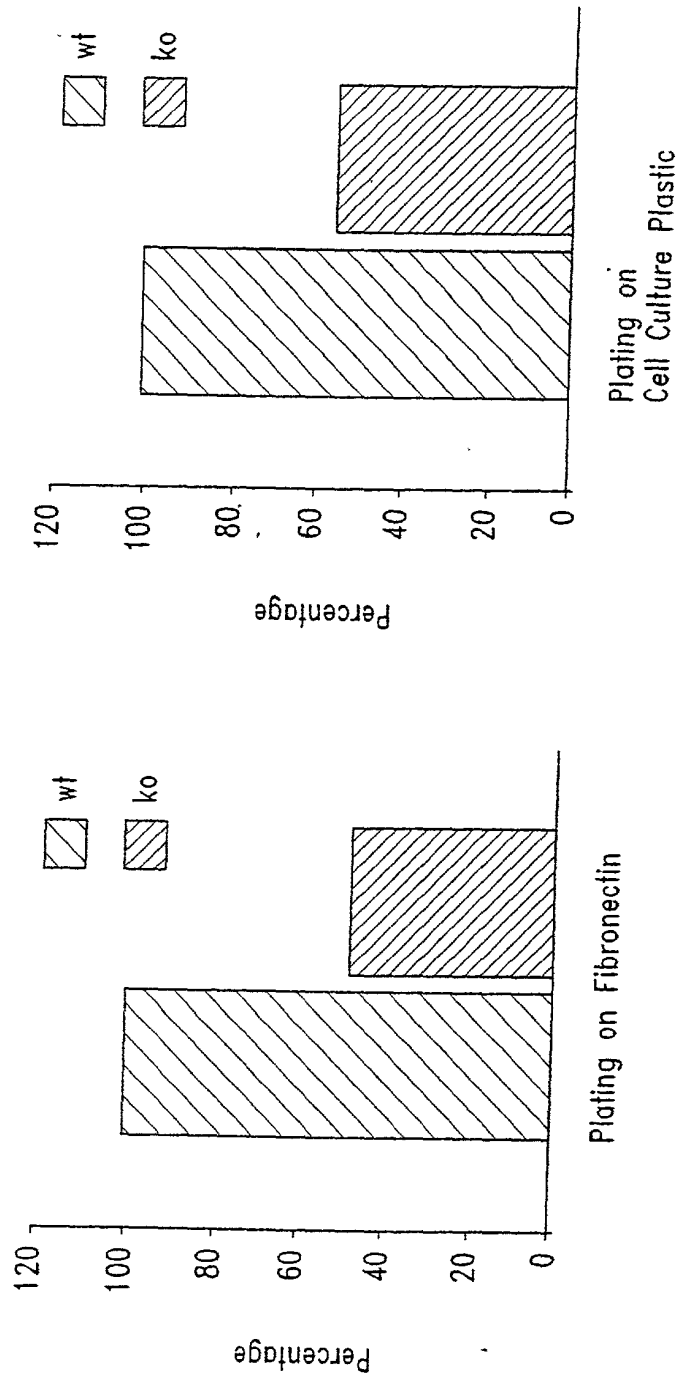


Fig. 29

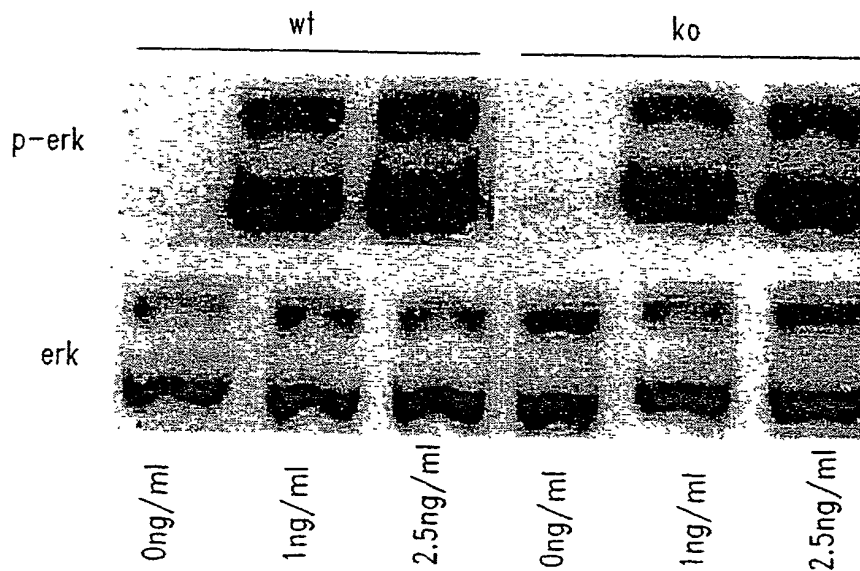
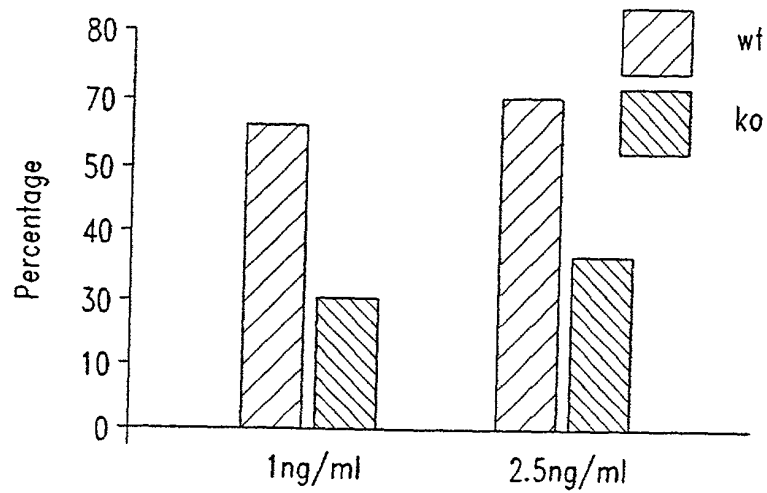


Fig. 30

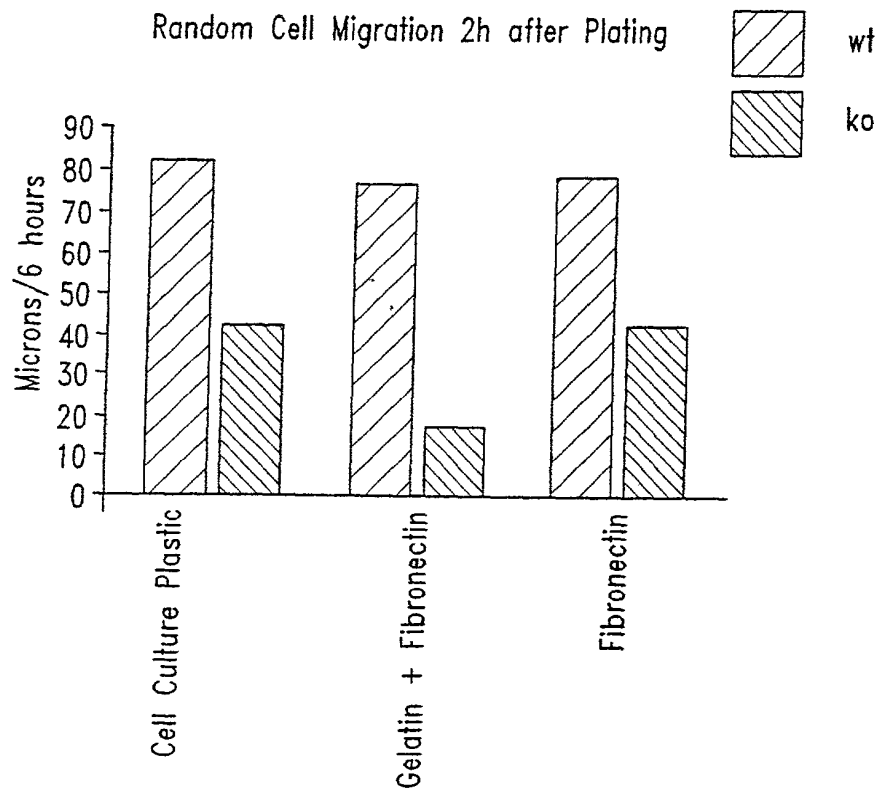


Fig. 31



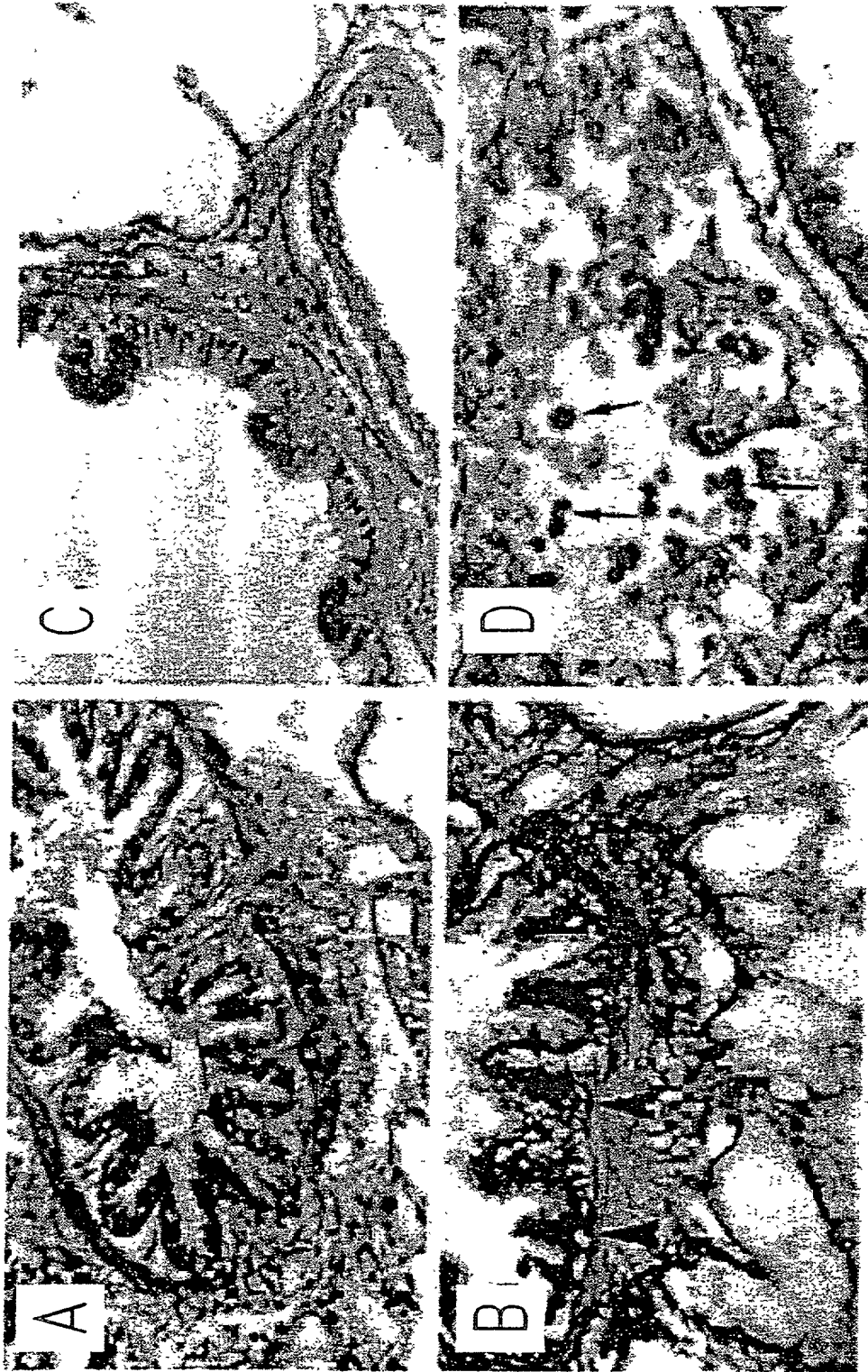
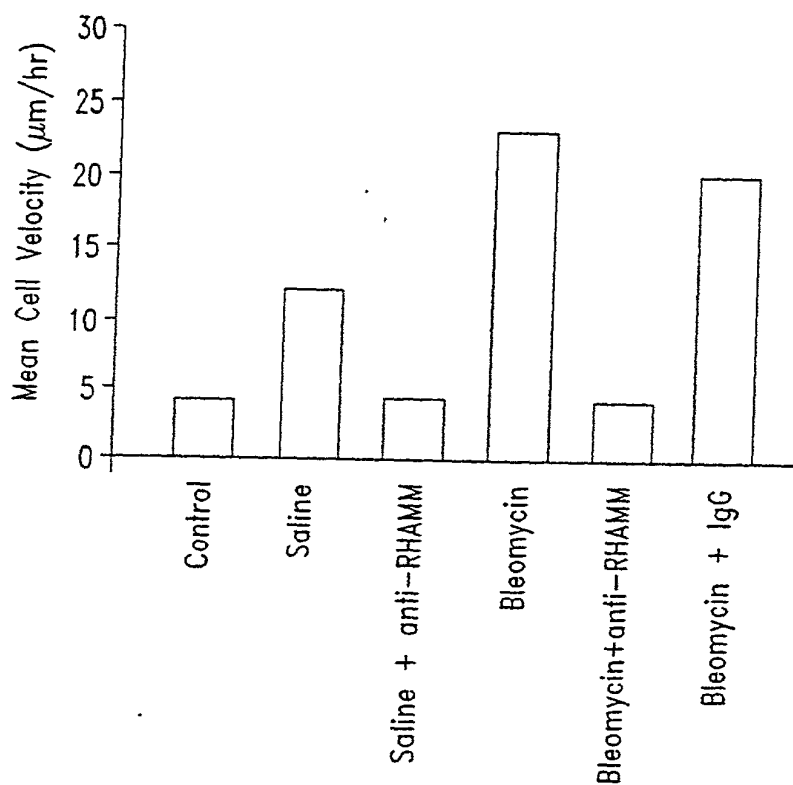
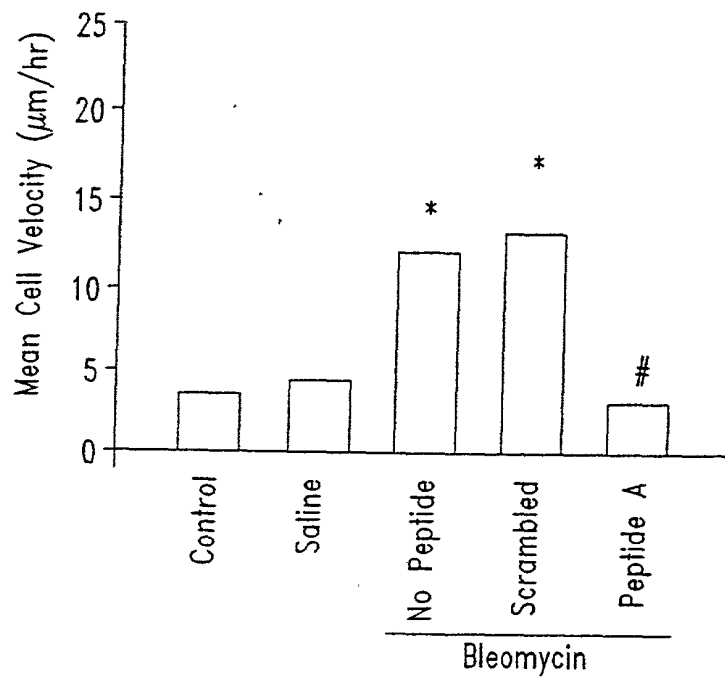


Fig. 32



*Fig. 33*



*Fig. 34*

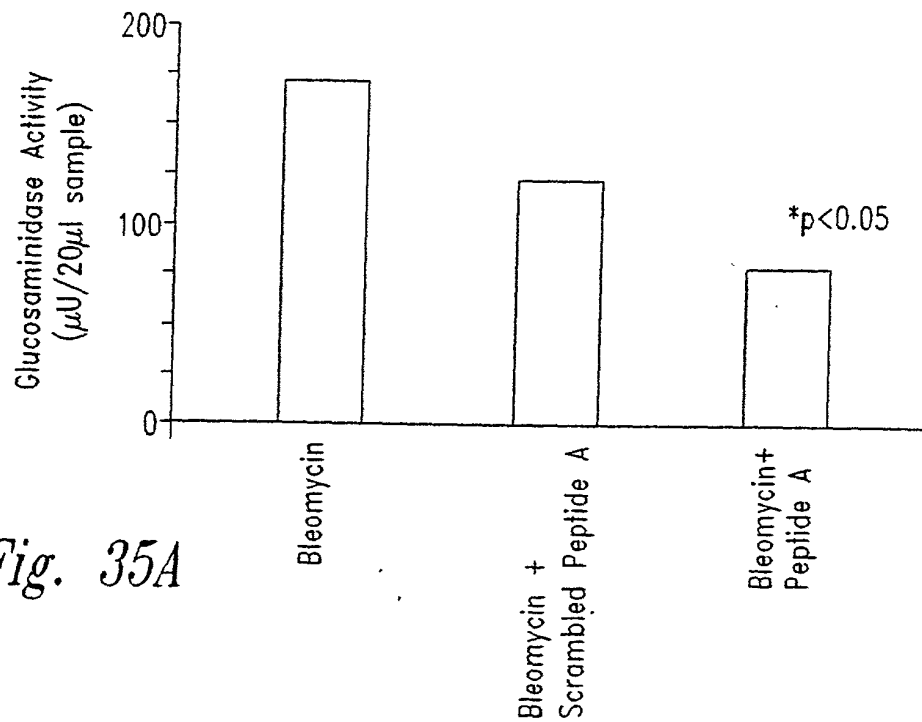


Fig. 35A

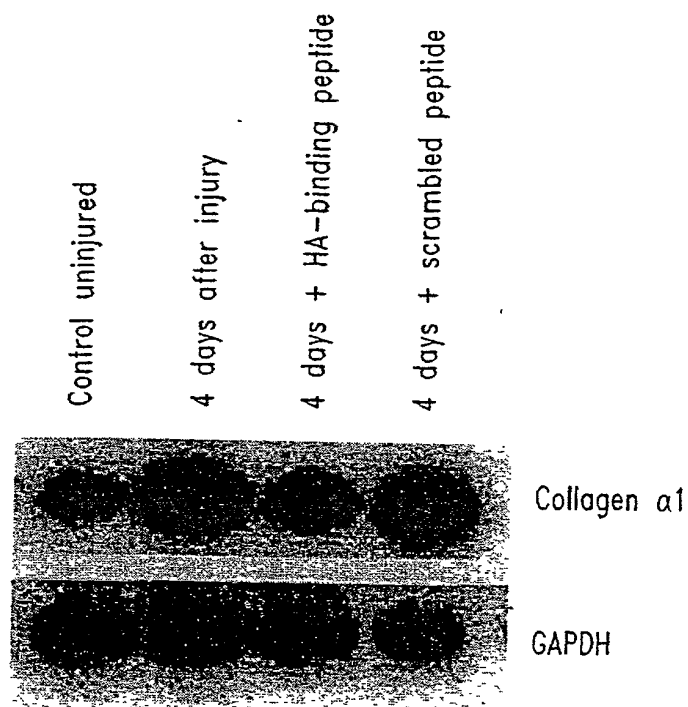


Fig. 35B

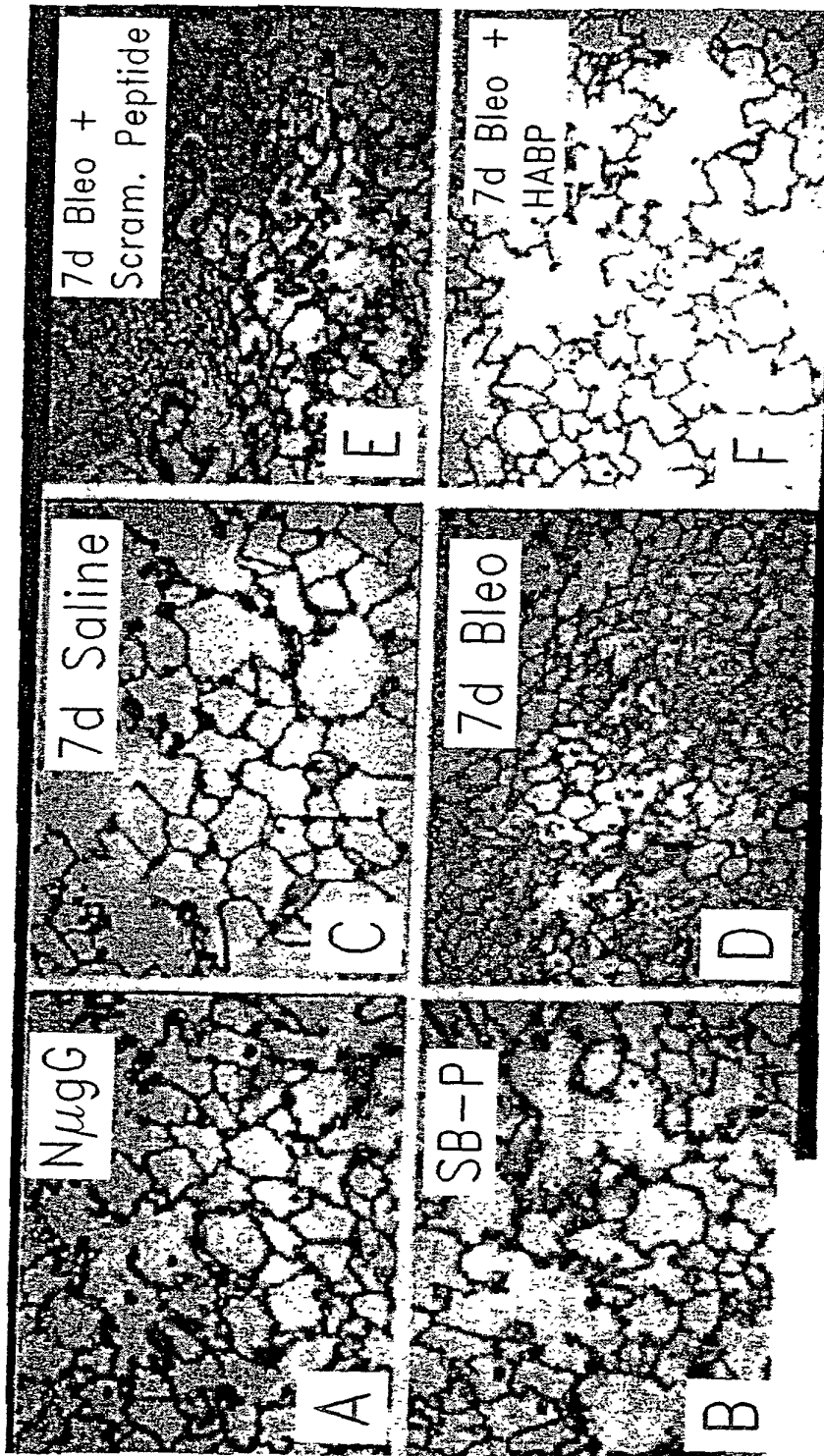
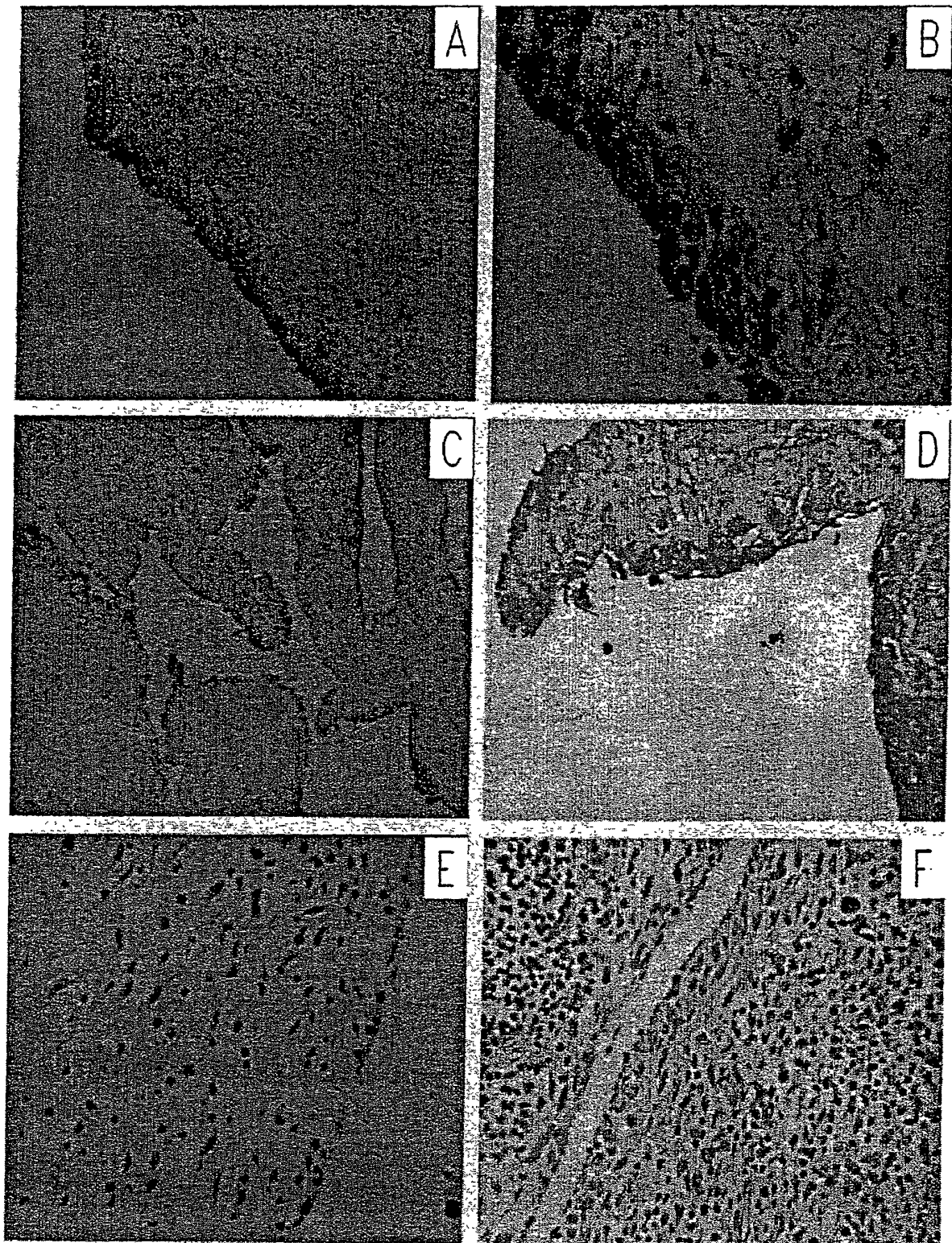


Fig. 36

Patient	% of total X4+ cells	% of total V5+ cells	Neutrophils		Monocytes/macrophages		T cells		
			% of total cells	% of X4+ cells	% of V5+ cells	% of total cells	% of X4+ cells	% of V5+ cells	% of V5+ cells
W.H.	ND	50.7	70.5	81.2	ND	21.8	87.1	66.4	11.7
M.T.	74.6	20.7	80.7	ND	9.9	11.2	89.6	ND	<2.0
L.S.	43.9	34.4	ND	ND	ND	8.5	ND	53.8	5.3
S.M.	67.6	4.0	67.3	80.9	ND	ND	ND	ND	10.0
M.M.	19.2	19.6	25.2	68.3	ND	ND	ND	ND	4.5
D.D.	35.7	31.2	40.7	99.3	ND	ND	ND	ND	<2.0
P.B. (r)	77.4	71.8	ND	ND	ND	9.2	99.8	88.3	13.0
P.B. (l)	85.0	82.3	ND	ND	ND	12.8	99.4	58.3	11.0
S.L.	51.6	45.5	61.7	92.1	77.2	8.8	73.4	85.6	6.0
R.C.	10.6	6.7	54.1	63.8	13.8	5.6	50.3	43.9	8.5
N.N.	27.9	10.3	44.1	54.6	21.4	3.5	77.1	49.4	33.1
M.G.	85.48	84.63	86.7	99.6	99.5	5.52	98.7	98.9	4.8

- ND - non-determined
- (r) - right knee
- (l) - left knee

Fig. 37



*Fig. 38*

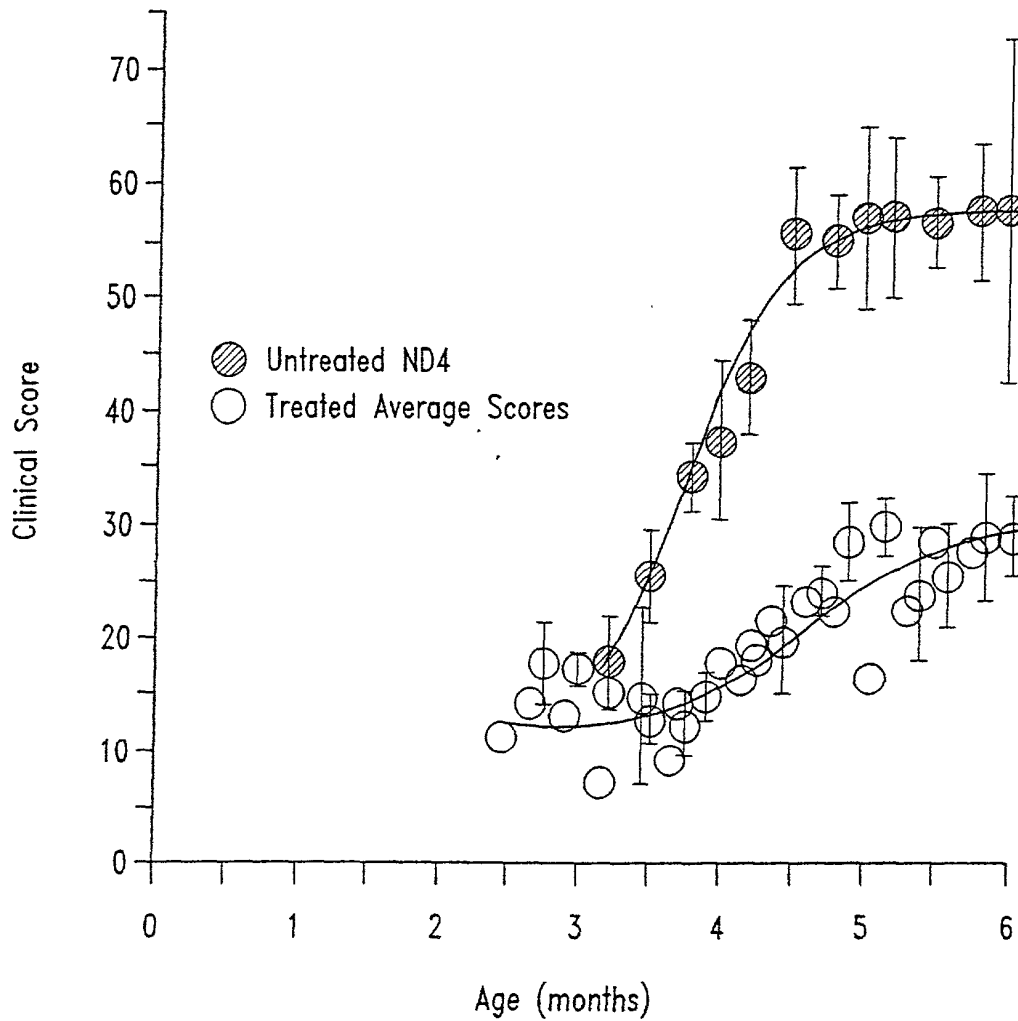


Fig. 39



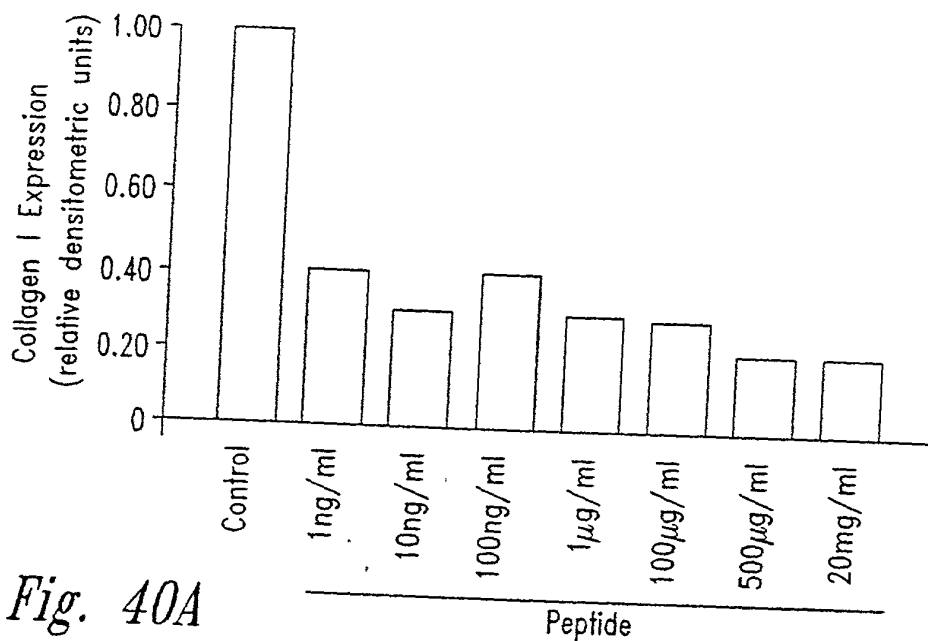


Fig. 40A

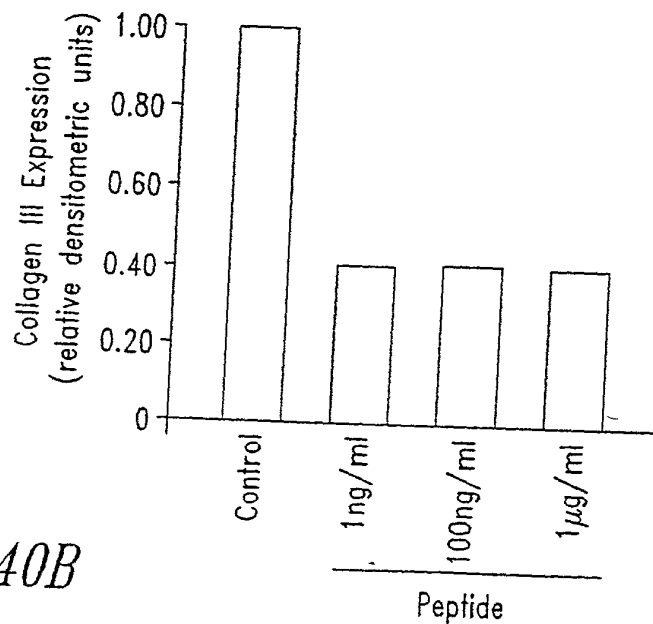


Fig. 40B

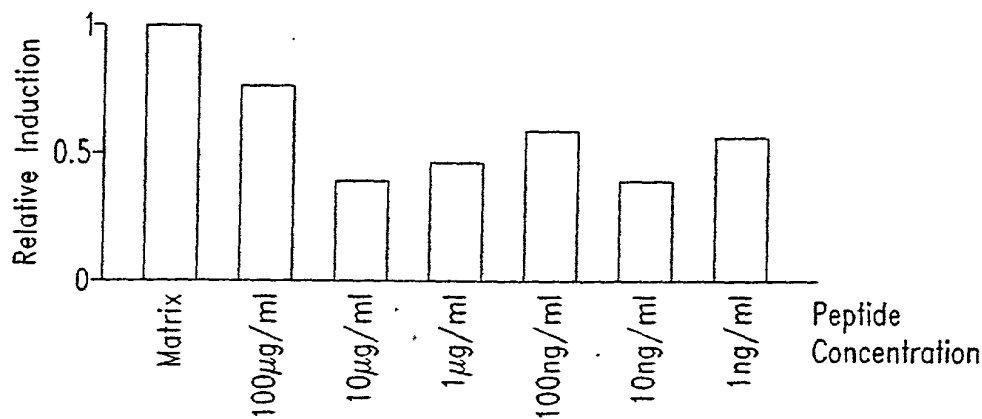
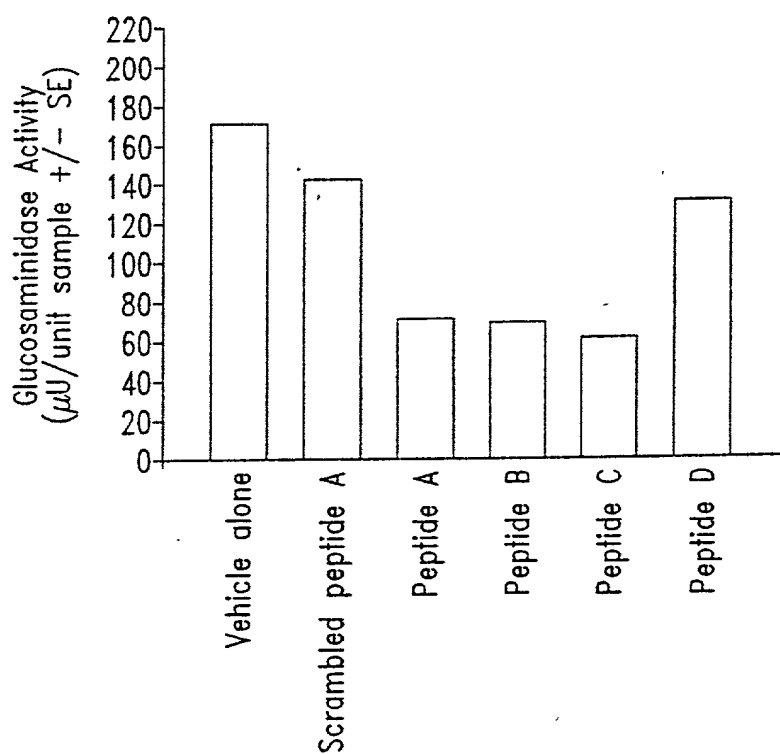
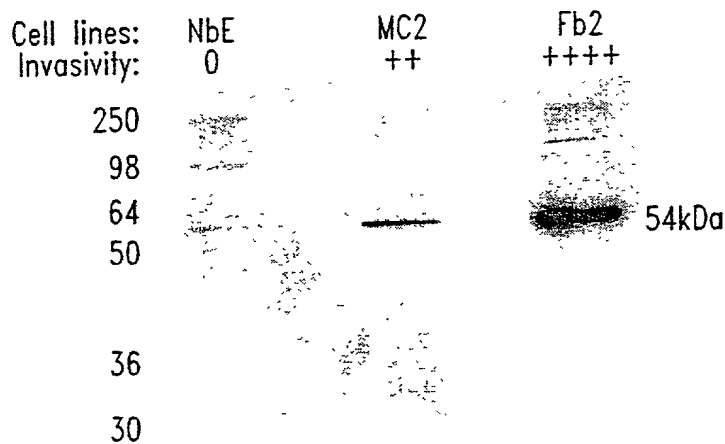


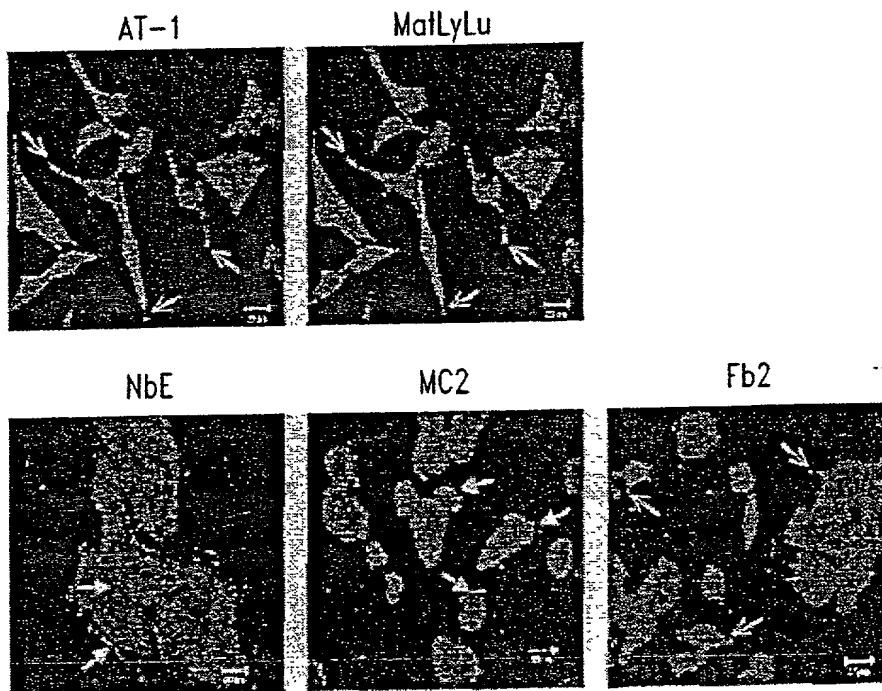
Fig. 41



*Fig. 42*



*Fig. 43A*



*Fig. 43B*

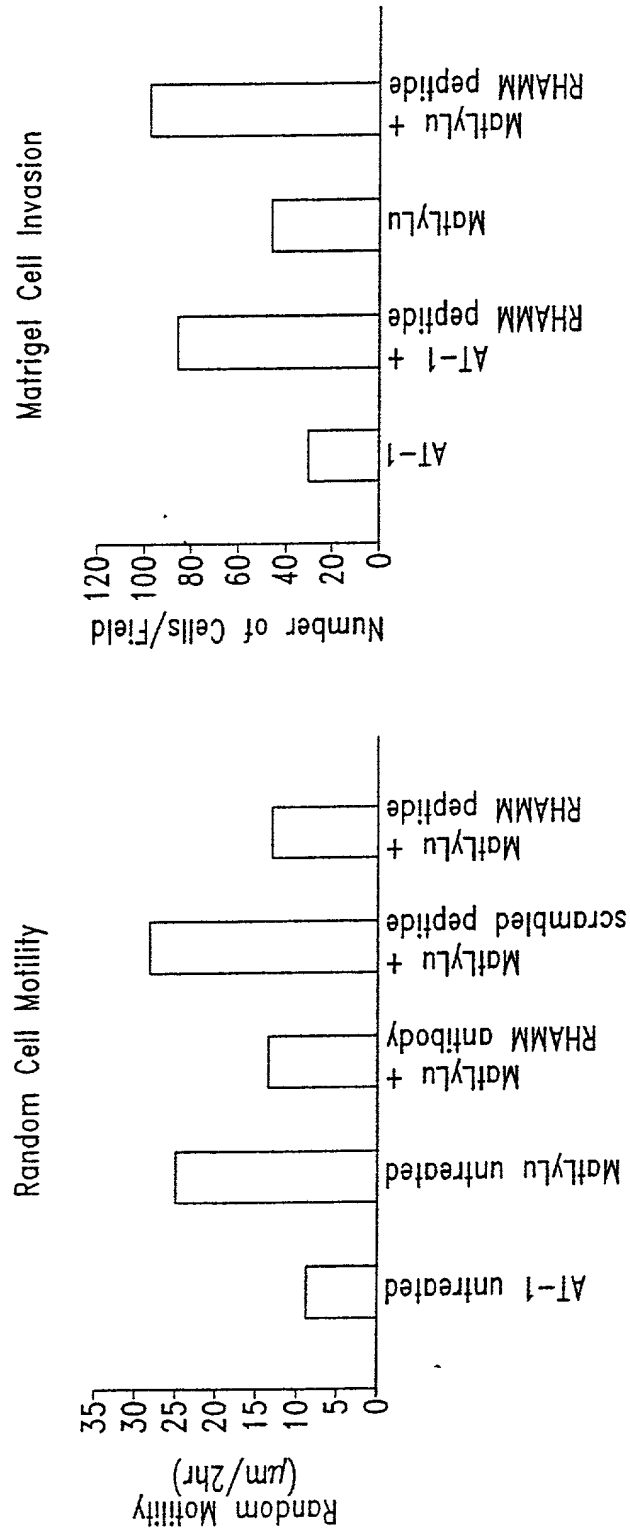
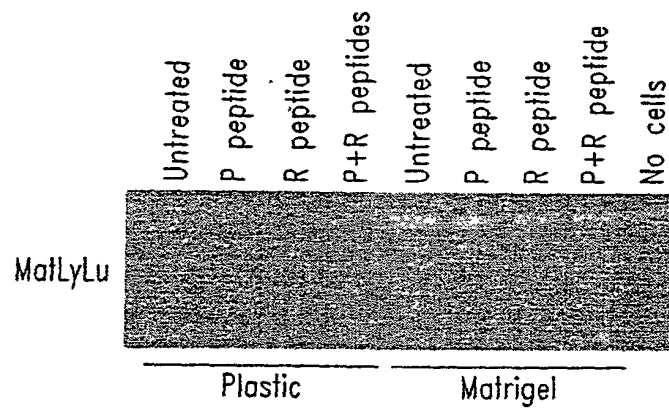
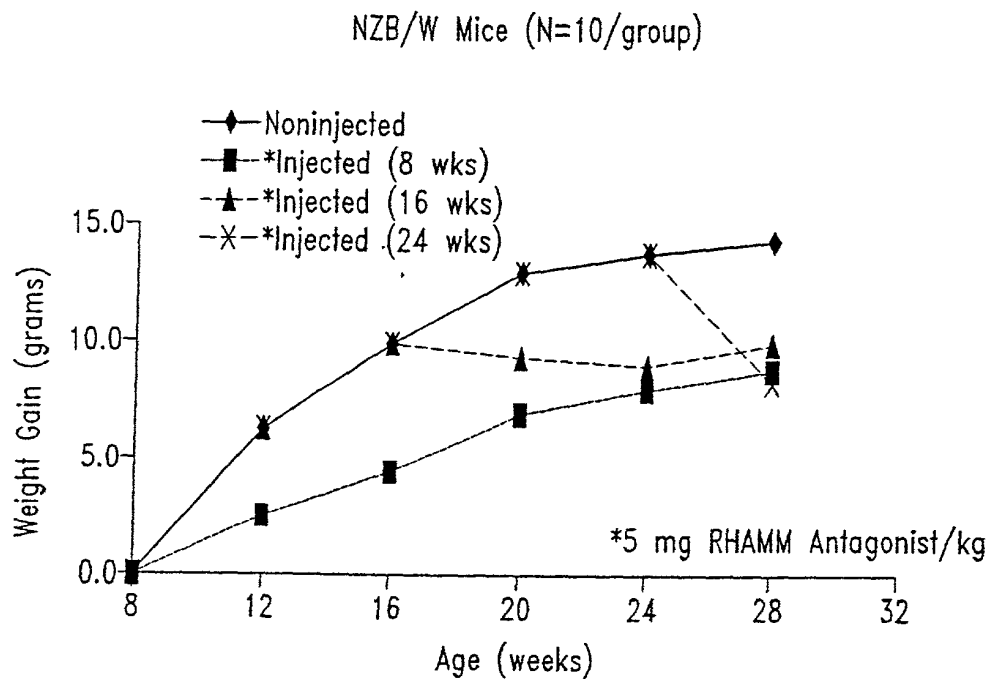


Fig. 44A

FIG. 44A

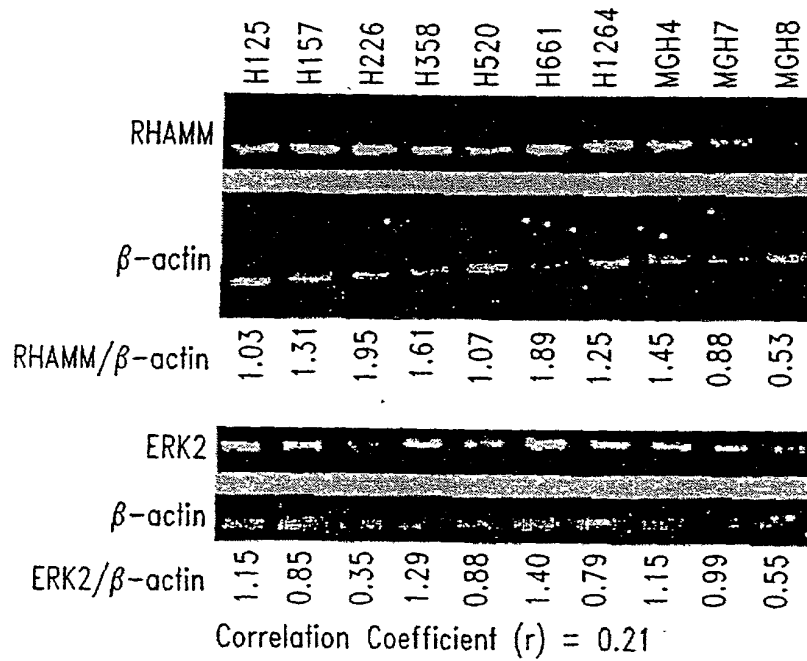


*Fig. 44B*

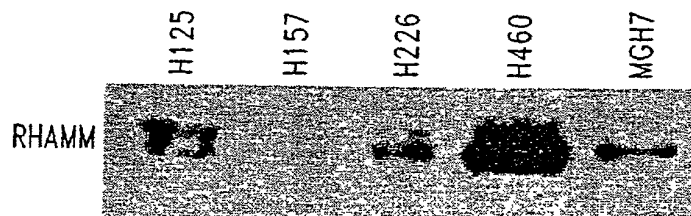


Note: This effect is not being seen with NOD mice

*Fig. 45*

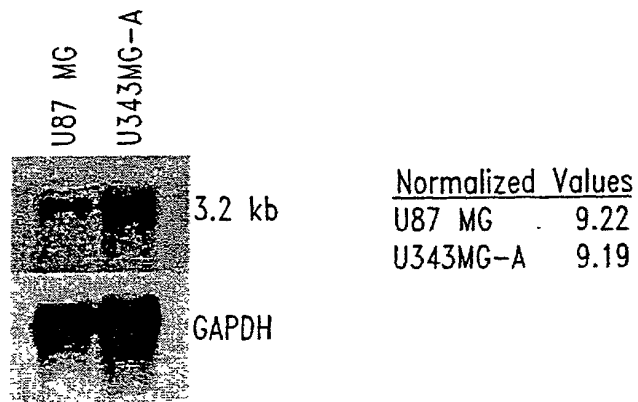


*Fig. 46A*

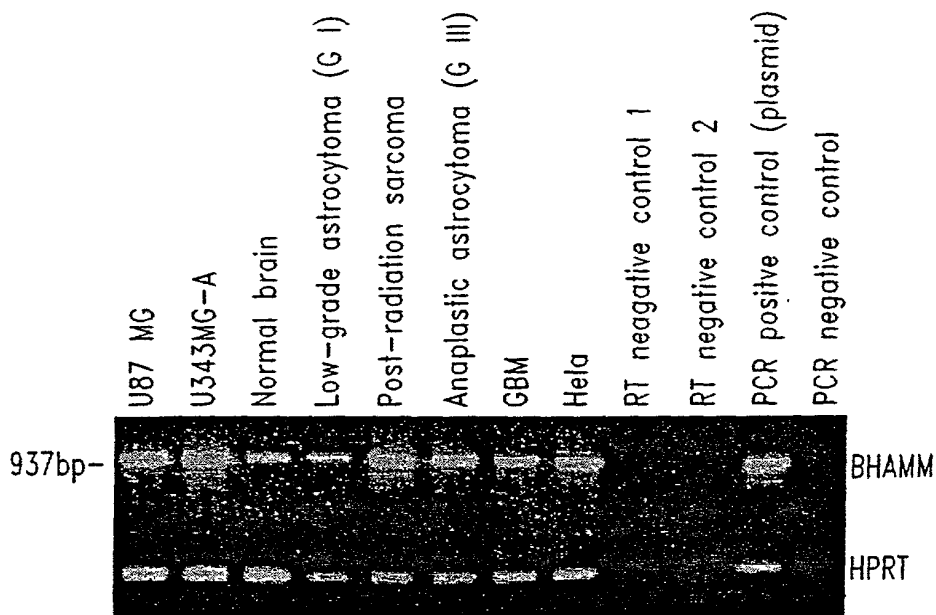


*Fig. 46B*

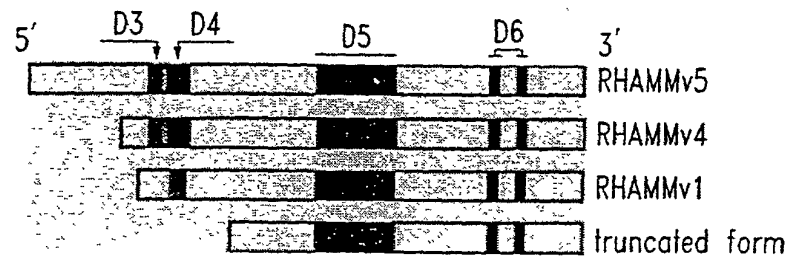




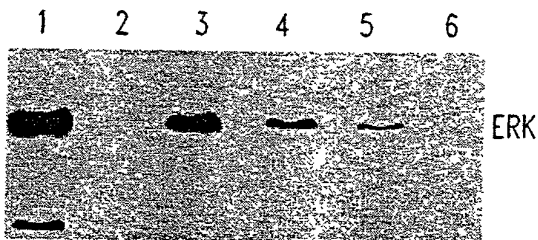
*Fig. 47A*



*Fig. 47B*



*Fig. 48A*

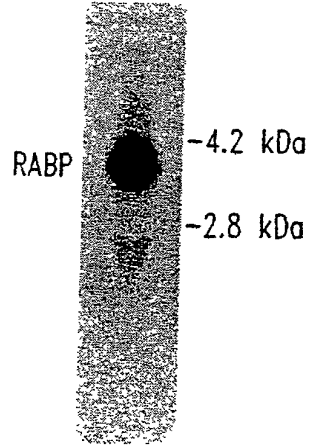


*Fig. 48B*

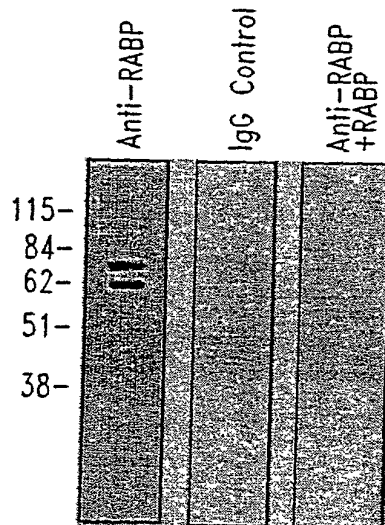
RHAMM binding protein cDNA (RABP) (partial)

GAA TTC GCG GCG GCG TCG ACC AAC AAG CCC CCT GCT GTT TCC CCG GGG  
E F A A A S T N K P P A V S P G  
GTG GTC TCC CCA ACC TTT GAA CTT ACA AAT CTT CTA AAT CAT CCT GAC  
V V S P T F E L T N L L N H P D  
CAT TAT GTA GAA ACA GAG AAC ATT CAG CAT CTC ACA GAC CCG GCT CTA  
H Y V E I E N I Q H L T D P A L  
GCA CAT GTG GAT AGA ATA AGC GAA GCC CGG AAA CTG AGT ATG GGA TCT  
A H V D R I S Q A R K L S M G S  
GAT GAT GCT GCC TAC ACA CAA GCT CTG CTG GTG CAC CAG AAG GCC AGG  
D D A A Y T Q A L L V H Q K A R  
ATG GAA CGG CTT CAA AGA GAG CTC GAG ATG CAA AAG AAA AAG CTG GAT  
M E R L Q R E L E M Q K K K L D  
AAA CTC AAA TCT GAG GTC AAT GAG ATG GAA AAT AAT CTA ACT CGA AGG  
K L K S E V N E M E N N L T R R  
CGC CTG AAG AGA TCA AAT TCC ATT TCC CAG ATA CCG TCA CTC GAA GAA  
R L K R S N S I S Q I P S L E E  
ATG CAG CAG TTG AGA AGT TGT AAT AGA CAA CTC CAG ATT GAC ATT GAC  
M Q Q L R S C N R Q L Q I D I D  
TTT GAC TGC TTA ACC AAA GAA ATT GCA TCT TTT TCA AGC CCG AGG ACC  
F D C L T K E I A S F S S P R T  
ACA TTT TAA CCC CAG CGC TAT TCA TAA CTT TTA TGA CAA TAT TGG ATT  
T F \*  
TGT AGG CCC TGT GCC ACC AAA ACC CAA AGA TCA AAG GTC CAC CAT CAA  
AGG TCG ACG CGG

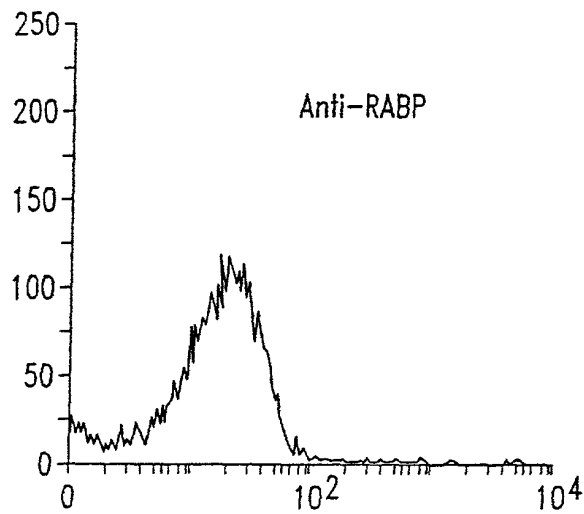
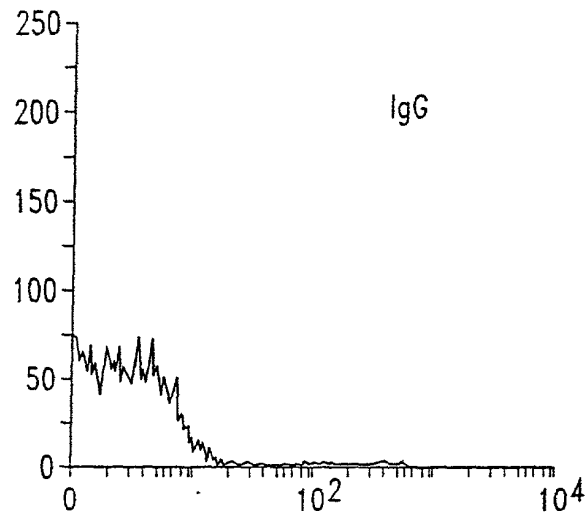
Fig. 49A.



*Fig. 49B*



*Fig. 49C*



*Fig. 49D*

Human: 1 MSFPKAPLKRFPNDPSGAPSPGAYDVKTLEVLKGPVSFQKSQRFKQKQESKQNLNVDKDTTLPASARKVKSSESK

Human: 76 KESQKNKDLKILEKEIRVLLQERGAQDRRIQDLETELEKMEARLNAALREKTSLSANNATLEKQLIELTRTNEL

Human: 151 LKSKFSENGNQNLRLSLELMKLRNKRETKMRGMMAKQEGMEMKLQVTRQSLEESQKGIAQLEGKLV<sup>+</sup>IEKEKI  
 Mouse: 1 MRALSLELMKLRNKRETKMRSMVMVKQEGMELKLQATQKDLTESKGI<sup>+</sup>VQLEGKLV<sup>+</sup>IEKEKI

Human: 226 DEKSETEKLEYIEEISCASDQVEKYKLDIAQLEENLKEKND<sup>+</sup>EILSLKQSL<sup>+</sup>EENIVILSKQVEDLNVKQ<sup>+</sup>Q<sup>+</sup>LEKE  
 Mouse: 63 DEKCETEKLEYIQEISCASDQVEKCKVDIAQLEEDLKEKDREILSLKQSL<sup>+</sup>EENITF-SKQIEDLTVKQ<sup>+</sup>Q<sup>+</sup>LETE

Human: 301 KEDHVNRRNHNENLNAEMQN<sup>+</sup>LKQKFILEQQEHEK<sup>+</sup>LQKELQIDSL<sup>+</sup>LQKEK<sup>+</sup>SSSLHQKLCFQ<sup>+</sup>EE<sup>+</sup>VMKEKNLF  
 Mouse: 138 RNDLVSKDRERAETLSAEMQILTERLALERQEYK<sup>+</sup>LQKELQSQSL<sup>+</sup>LQKEK<sup>+</sup>SARLQQQLCSFQ<sup>+</sup>EE<sup>+</sup>MTSEKNVF

Human: 376 EEELKQTLDEL<sup>+</sup>DKLQKEEQAERLVKQLEEEAKSRAEELK<sup>+</sup>LLEEK<sup>+</sup>LKGKEAEKSSAAHTQATLLL-----  
 Mouse: 213 KEELKALAE<sup>+</sup>LDAVQKEEQSERLVKQLEEEKSTA<sup>+</sup>EQLTRLDNLLREKEVELEKHIAAHQA<sup>+</sup>ILIAQEKYNDTA

Human: -----

Mouse: 288 QSLRDVTAQLESVQEKYNDTAQSLRDVTAQLESEQEKYNDTAQSLRDVTAQLESEQEKYNDTAQSLRDVTAQLES

Human: 443 QEKYDSMVQSL<sup>+</sup>EDVTAQFESYKALTASEIEDLKLE<sup>+</sup>SSLQEKAAKAGKNAEDVQH<sup>+</sup>QILATESSNQ<sup>+</sup>EYVRMLDLQ  
 Mouse: 363 QEKYNDTAQSLRDVTAQLESYSSTLKEIEDLKLENL<sup>+</sup>TLQEKVAMAEKSVEDVQQILTAESTNQ<sup>+</sup>EYARMVDLQ

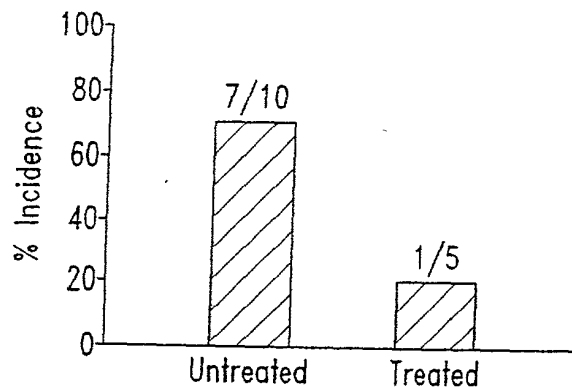
Human: 518 TKSALKETEIKEITVSFLQKITDLQNQLKQ<sup>+</sup>QEE<sup>+</sup>DFRKQLEDEEGRKAEKEN<sup>+</sup>TTAELTEEINKWRLLYEELYNKTK  
 Mouse: 438 NRSTLKEEEIKEITSSFLEKITDLKNQLRQ<sup>+</sup>QDEDFRKQLEEKGR<sup>+</sup>TAEKENVMTEL<sup>+</sup>TMEINKWRLLYEELYEYKTK

Human: 593 PFQLQDAFEVEKQALLNEHGAAQEQLNKIRDSYAKLLGHONLKQKIKHVVKLDENSQ<sup>+</sup>LKSEVSKLRQ<sup>+</sup>LAKKK  
 Mouse: 513 PFQQQLDAFEAEKQALLNEHGATQEQLNKIRDSYAQLLGHONLKQKIKHVVKLDENSQ<sup>+</sup>LKSEVSKLRSQ<sup>+</sup>LVKRRK

Human: 668 QSETKQEE<sup>+</sup>LNKVLGIKHFDPSKAFHHESKENFALKTPLKEGNTN<sup>+</sup>CYRAPMECQESWK\*  
 Mouse: 588 QNELRQGE<sup>+</sup>LKALGIRHFDPSKAFCHASKENF---TPLKEGNPNCC\*

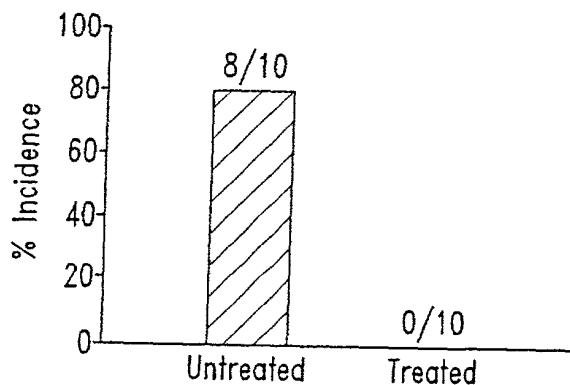
Fig. 50

05/03/09 10:50



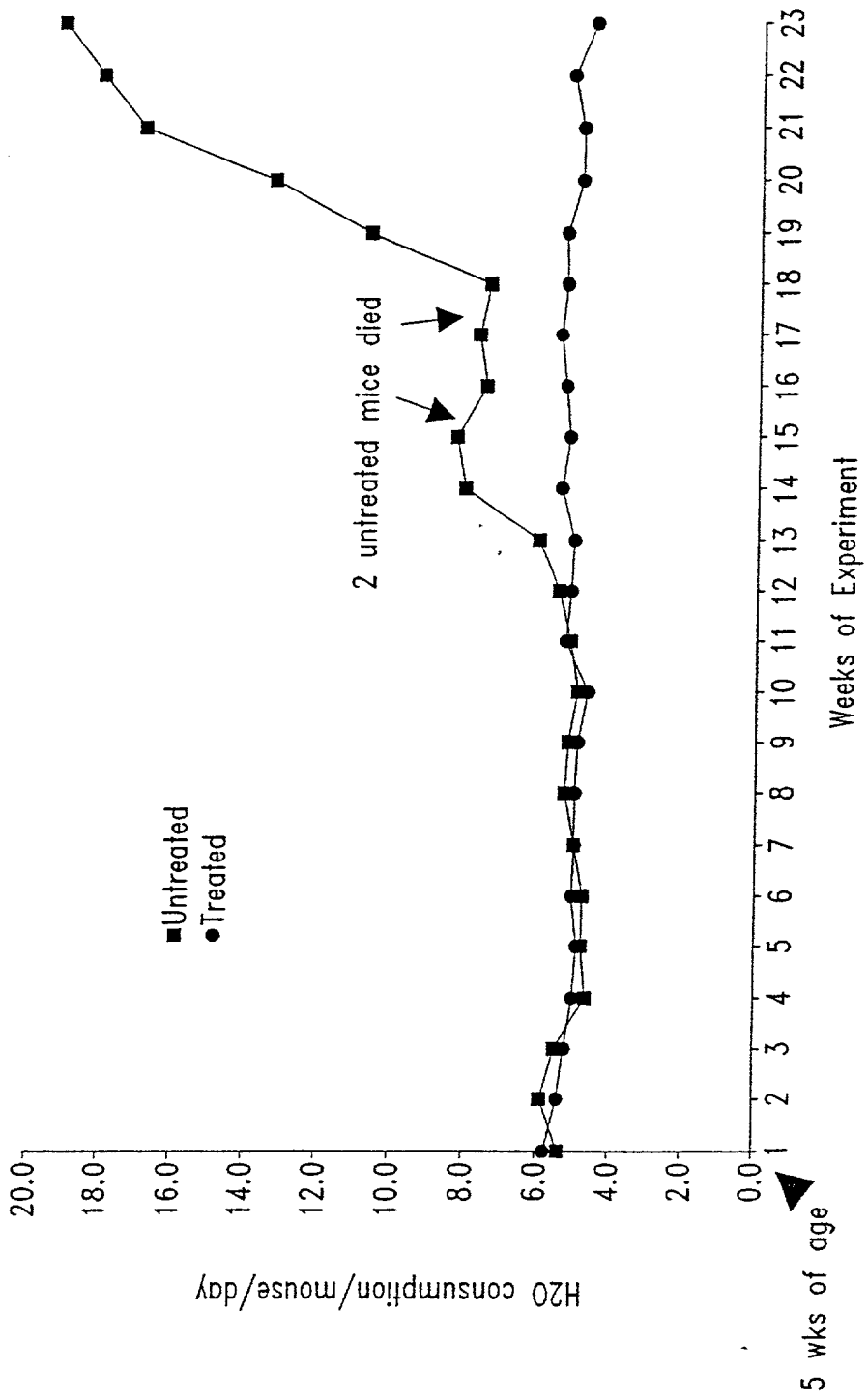
Note: normal blood glucose level = 99-140  
Incidence of abnormal blood glucose level in NOD mice

*Fig. 51*



Incidence of abnormal urine glucose level in NOD mice

*Fig. 52*

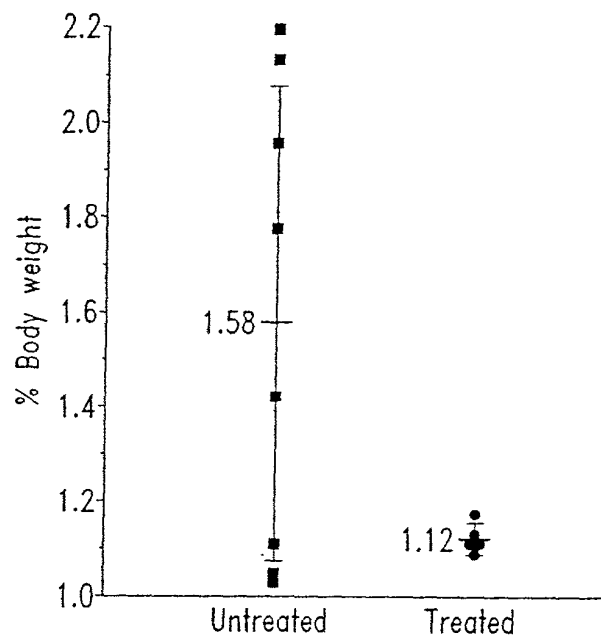


Note: Increased H2O consumption indicative of Diabetes Insipidus, a complication of Diabetes Mellitus

Effect of P-16 peptide on water consumption in NOD mice

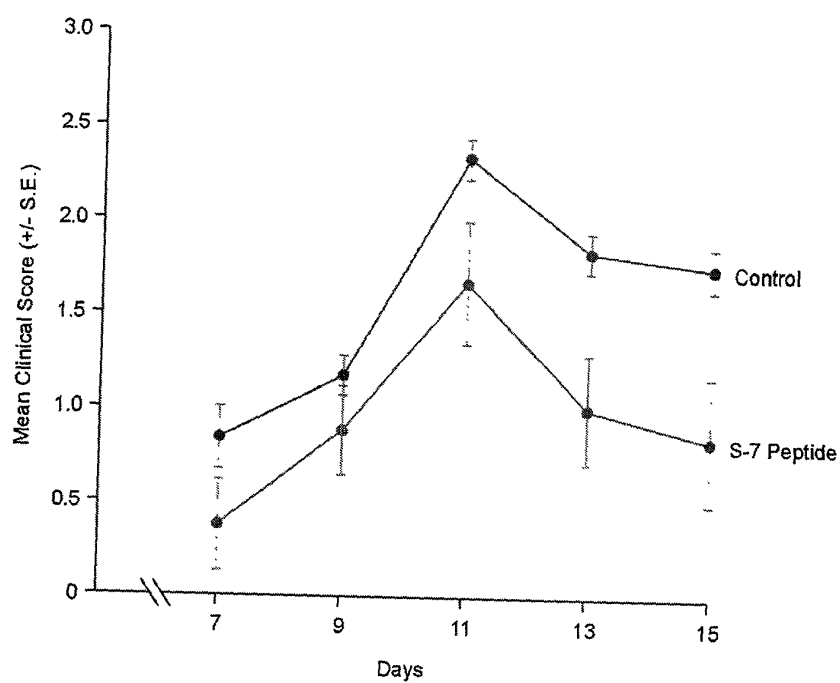
Fig. 53



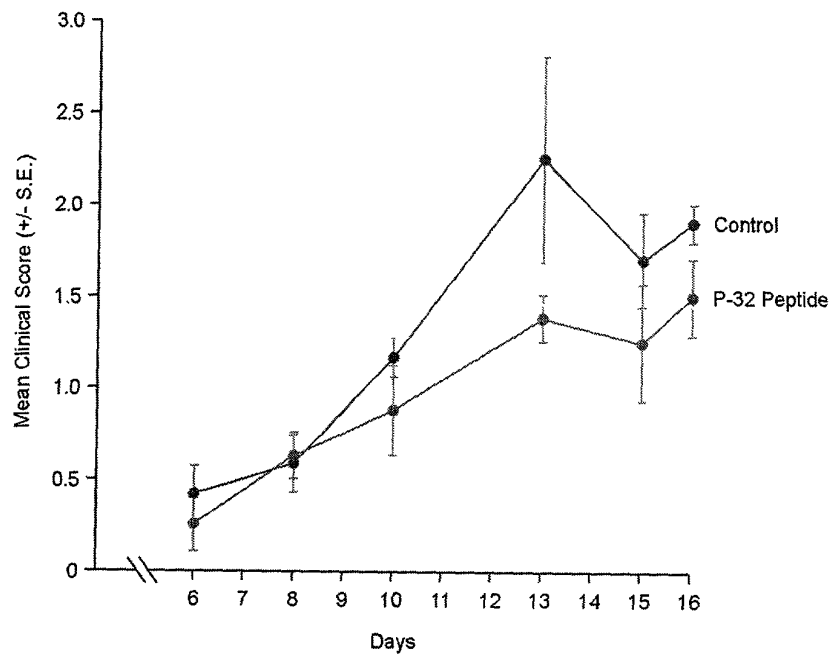


Note: 2 untreated animals died during the course of experiment  
Effect of P- 16 peptide on kidney weight in NOD mice

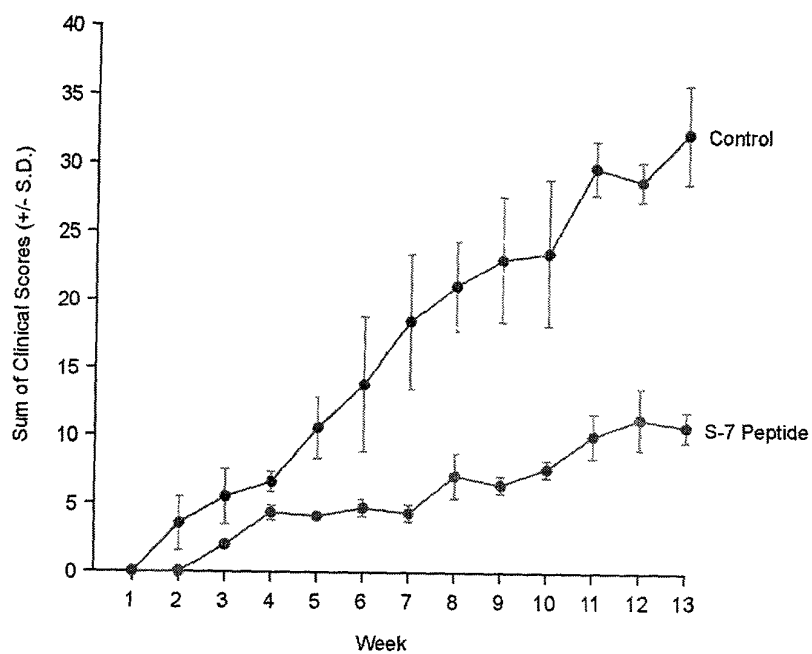
*Fig. 54*



*Fig. 55*



*Fig. 56*



*Fig. 57*

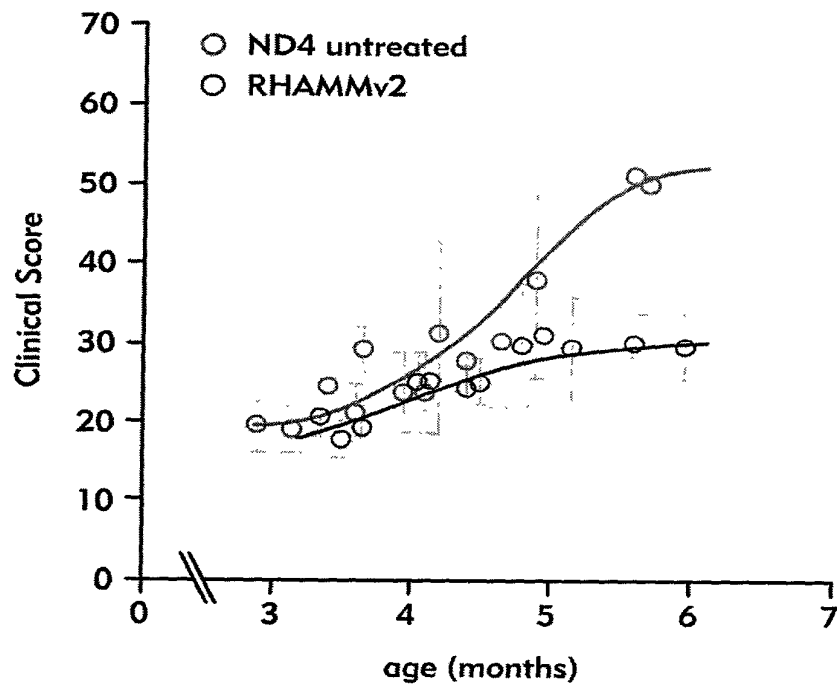
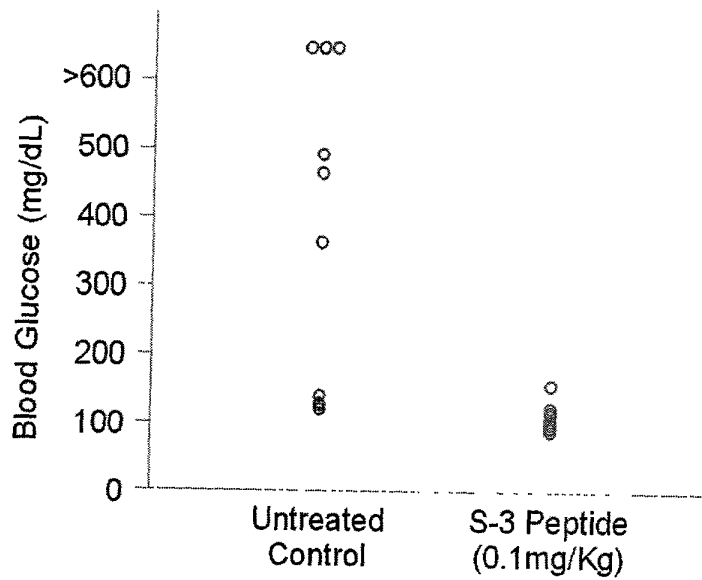
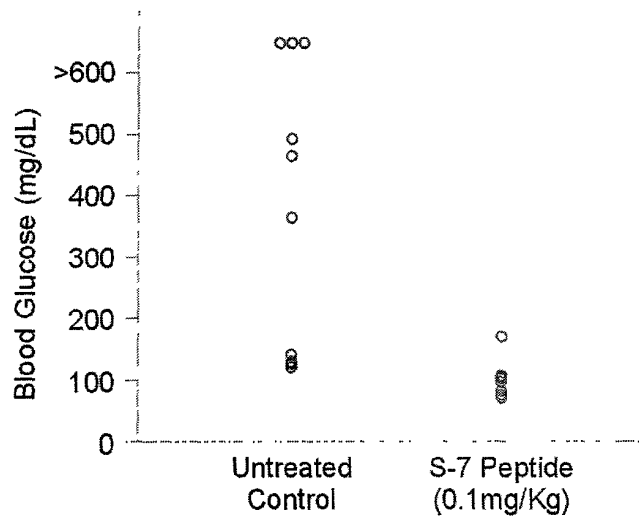


Fig. 58



*Fig. 59.*



*Fig. 60*